ELECTRONIC EFFECTS OF SUBSTITUENTS IN AROMATIC NITRATION

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G. J. Wright

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ABSTRACT

Product distributions from the nitration of toluene, o-xylene, m-xylene, hemimellitene and pseudocumene have been determined in nitric acid-acetic anhydride mixtures, nitronium tetrafluoroborate-sulpholane mixtures and in the nitric acid-sulphuric acid-nitromethane system. The Additivity Principle is applied to the toluene results to calculate product ratios for the other hydrocarbons. Comparison of calculated and experimental results shows this to be an unsatisfactory method of calculating product distributions for these reactions. The differences between calculated and experimental results are examined quantitatively in terms of modified ortho substituent constants.

Mixtures of nitric acid in acetic anhydride are shown to bring about direct acetoxylation of the aromatic nucleus when activated by more than one methyl group. The acetoxylation reaction has the characteristics of an electrophilic substitution reaction with large steric requirements and high selectivity. An estimate of the Hammett rho for the reaction is made.

Product distributions from the nitration of indan and tetralin in the three nitrating systems have also been determined. These results are discussed in terms of the Mills-Nixon effect. An explanation for these and the results of other investigations of indan and tetralin is presented.

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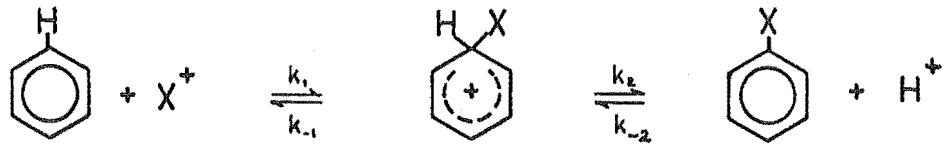
INTRODUCTION

The Additivity Principle has been used successfully to predict the rates of electrophilic substitution of the methylbenzenes in a number of reactions. This thesis examines the usefulness of the Principle in predicting the product distributions arising from the nitration of these hydrocarbons, by comparing calculated and experimental product ratios. Product distributions from the hydrocarbons indan and tetralin are also discussed as evidence for the nature of the Mills-Nixon effect. During the course of the work, mixtures of nitric acid and acetic anhydride were found to bring about direct acetoxylation of the aromatic nucleus, and a study of this reaction is made.

The work forming the background to the investigation is described in this Introduction. A brief outline of the mechanism of electrophilic aromatic substitution with special reference to nitration is given, and the nature of the nitrating species in the three reaction systems used is discussed. The Additivity Principle is reviewed and the history of the Mills-Nixon effect described.

The mechanism of electrophilic aromatic substitution.

It is now generally accepted that the majority of electrophilic aromatic substitution reactions proceed via a σ-complex, or Wheland intermediate[1] (I) and that the reaction may be represented as follows:



I

Such a mechanism implies that while the energy profile for attack by different reagents may vary somewhat, the general shape and the reaction coordinates are very similar.[2] The σ-complex is not a transition state; it is better regarded as a more or less stable intermediate which for certain reactions at least, appears to have been successfully isolated. Objections to an intermediate of this type were raised on the grounds that loss of the full resonance energy of the benzene ring would make the σ-complex very unstable, but it has been pointed out[3] that stabilisation is in part restored by the energy of formation of the Ar-X bond, and by hyperconjugation of the hydrogen, and possibly the electrophile, with the residual conjugated system. Such a reaction scheme would present different kinetic behaviour and substituent effects depending on the relative

magnitudes of the various k values.

The reaction profile for such reactions is generally drawn with the σ-complex occupying a valley between two transition states--one for the formation of and the other for the destruction of the σ-complex. The relative heights of the two transition states determines whether formation of the Ar-X bond or rupture of the Ar-H bond is rate-determining. Hammond[4] has postulated that the σ-complex is a good model for both transition states, and that conversion between any of these requires only very small changes in molecular parameters. This postulate is generally assumed to be correct in most discussions of the nature of the transition state.

A considerable body of experimental evidence is available to support this mechanism. The kinetic isotope work pioneered by Melander[5] has proved capable of delicate investigation into the nature of the reaction profiles. Substitution of H^2 or H^3 for the departing H^1 produces a significant change in rate (generally by a factor of four and greater) if the second transition state is appreciably higher than the first. When no such primary isotope effect is observed, smaller secondary effects can give useful information about the reaction pathway, though these effects may be difficult to interpret.[6] As an indication of the validity of Hammond's postulate, it has been pointed out[7] that practically all electrophilic

substitution reactions with the exception of nitration may proceed with an experimentally measurable isotope effect provided the right conditions are chosen.

Considerable progress has been made in the isolation of σ -complexes, sometimes under reaction conditions. This work, which is well reviewed by Berliner,[8] lends support to the intermediacy of such complexes in these reactions. Evidence is also available to show that $HCl-AlCl_3$ and $HF-BF_3$ systems form σ -complexes with aromatic systems, while HCl forms π-complexes in which interaction occurs between the HCl and the whole π - electron cloud of the aromatic system.[9] Comparisons of reactivity and " σ -complex" basicity show striking correlations, which are not exhibited by comparisons with " π -complex" basicity.[8]

Nitration of aromatic substrates has been extensively studied in many nitrating systems. This work, reviewed by de la Mare and Ridd,[10] has shown that the reaction profile below (Fig. 1), with a transition state T very close to the σ -complex, is a very satisfactory model for aromatic nitration.

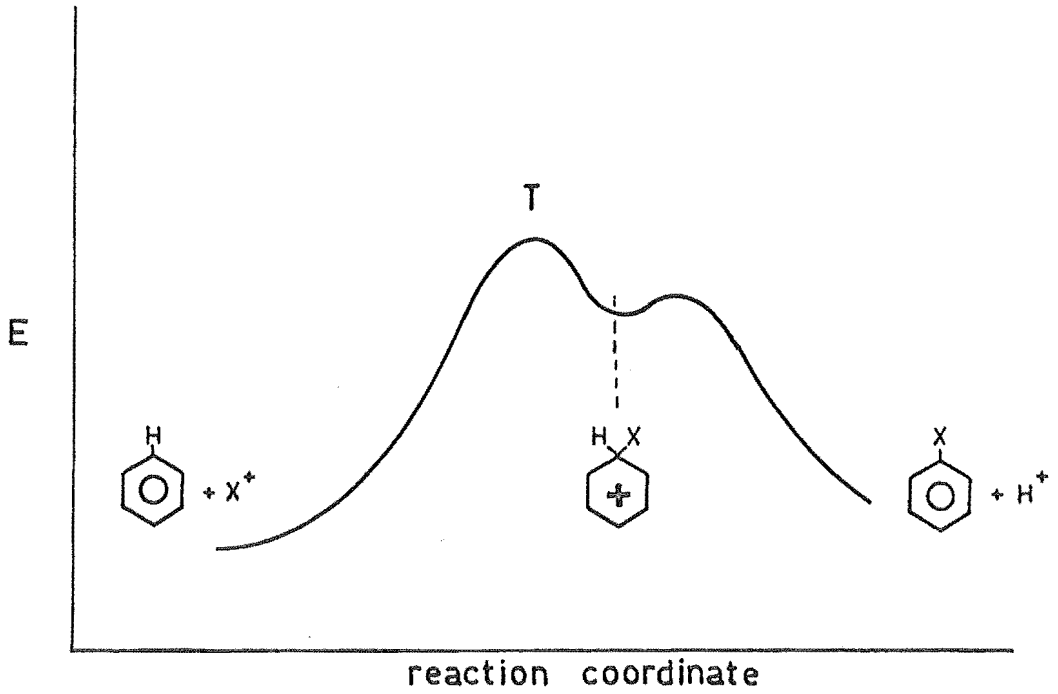


Fig. 1

The formation of π-complexes.

The existence of charge-transfer complexes, or π-complexes, between aromatic hydrocarbons and electron acceptors is well-established.[8] The interaction between the aromatic π-electron cloud and the acceptor molecule leads to a complex of low stability which cannot normally be isolated, and the existence of such compounds is generally inferred from physical measurements made on solutions. A few π-complexes like picrates and trinitrobenzene derivatives are particularly stable and can

be isolated. The most intensively studied π -complexes are those formed between benzene and the halogens or HCl. The HCl-aromatic systems, in which 1:1 complexes are formed,[9,11,12] show properties consistent with an aromatic π -electron system which has undergone little distortion in forming the complex.

Dewar was the first to propose that π -complexes were involved in electrophilic aromatic substitution to such a significant extent that their formation could become rate determining.[13] Dewar's case rested mainly on the known formation of such complexes, but as in the case of σ -complexes, this is not sufficient evidence for their participation in the rate-determining step. Furthermore, ΔH_f values for π -complex formation are usually much lower than activation energies in substitution reactions, and the complexing ability of the halogens is known to be the reverse of their electrophilic reactivity.[14] Proto-dedeuteration reactions have been considered to proceed through a π -complex transition state, but the σ -complex mechanism appears to explain the kinetic data equally well.[8] Zollinger[15] has shown that if steric hindrance to the formation of the σ -complex is too great the π -complex may become important; the iodination of 2-napthol-6,8-disulphonic acid appears to stop at the π -complex for this reason. The π -electron cloud of the aromatic system

has been shown to be distorted by substituents,[16] and the possibility of oriented π -complex intermediates has been considered.[17,18]

Until very recently most workers have restricted the role of π -complex formation in aromatic substitution to low energy intermediates with little effect on the overall rate. De la Mare has pointed out[10] that the importance of such complexes lies not in their effect on the activation energy, but in the fact that those factors which influence the stability and geometry of the π -complex may well also influence the nature of the σ -complex so that the latter becomes a poor model of the transition state. Melander carries this reasoning further.[19] By detailed analysis of the reaction profile and potential energy changes he shows that the formation of the π -complex can become rate determining if the electrophile and reagent are sufficiently reactive for the transition state to occur early in the reaction coordinate. According to this approach, a gradual change in the nature of the transition state from essentially a σ - to essentially a π -complex occurs as the reactivity of the system increases.

Olah and his collaborators[20] claim to have discovered a system in which the π -complex is a good model of the transition state. The work first reported involved the use of pre-formed nitronium ions as electrophiles, from the

reaction of $NO_2^+BF_4^-$ and related salts with aromatic substrates in organic solvents. The reactions proved to be extremely fast and showed the expected lack of discrimination between different hydrocarbons--i.e., low substrate selectivity. Isomer distributions obtained with such a reactive electrophile would be expected to approach the statistical values, but all hydrocarbons tested showed isomer distributions very similar to those obtained from conventional NO_2^+ nitrations. Typical results are shown in Table I.

TABLE I

Relative rates and product distributions from NO_2BF_4 nitrations.[20]

Hydrocarbon	Rate relative to benzene	Isomer distribution(%)		
		ortho	meta	para
benzene	1.00			
toluene	1.67	65.4	2.8	31.8
o-xylene	1.75	3-nitro 79.7		4-nitro 20.3
m-xylene	1.65	2-nitro 17.8		4-nitro 82.2
p-xylene	1.96			
mesitylene	2.71			
ethylbenzene	1.60	53.0	2.9	44.1
n-propylbenzene	1.46	51.0	2.3	46.7
i-propylbenzene	1.32	23.4	6.9	69.7
n-butylbenzene	1.39	50.0	2.0	48.0
t-butylbenzene	1.18	14.3	10.7	75.0

Olah explains these results in terms of a rate-determining π-complex transition state, and shows that the observed rates correlate well with the stabilities of known π-complexes but not with σ-complexes. The low substrate selectivity is explained by assuming that the whole π-system of the aromatic compètes for the electrophile--it is pointed out that π-complex stabilities are insensitive to the presence of substituents. Positional selectivity within each aromatic is assumed to arise from a second transition state of lower energy corresponding to the formation of the σ-complex. The height of this transition state differs for ortho, meta, and para substitution as it does in the conventional mechanism. The reaction profile drawn by Olah is shown in Fig. 2.

Other work by this group has extended this treatment to $AlCl_3$-CH_3NO_2-catalysed benzylation,[21] $FeCl_3$-catalysed bromination,[22] isopropylation,[23] $FeCl_3$ and $AlCl_3$-catalysed chlorination,[24] and t-butylations.[23,25] The electrophile in each case is considered to be markedly more active than "conventional" electrophiles. The fact that the nitration of halobenzenes by NO_2BF_4 shows closer similarity to conventional nitration than does nitration of alkylbenzenes is attributed to the lower π-electron density, and thus reduced π-complex forming ability in the halobenzenes.[20]

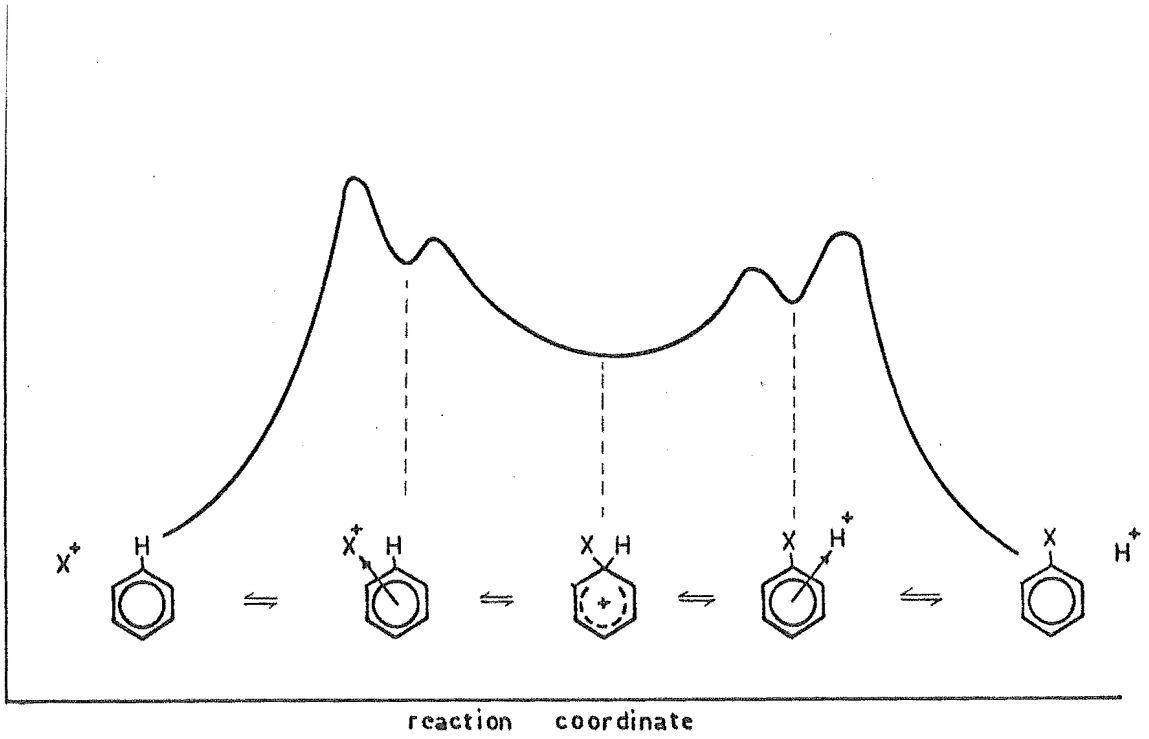


Fig. 2

The most serious objection which has been raised to this work[20] is that diffusion control of these very fast reactions would lead to similar lack of substrate selectivity. Olah reports extensive tests designed to show that the reactions are not diffusion controlled. It must therefore be assumed that these reactions provide examples of the rate-determining π-complex transition states predicted by Melander.

The position of the transition state on the reaction coordinate.

The preceding discussion has considered two extreme models for the rate-determining transition state in electrophilic aromatic substitution, the σ-complex and the π-complex. It has long been realised that the transition state of many such reactions is considerably different from the σ-complex, and Olah's work has served to emphasise the possibility of a gradual transition between the two extremes as the activity of the electrophile is changed. Two methods of estimating where the transition state for a given reaction lies between these two complexes are available. The first, the Extended Selectivity treatment developed by Brown,[26] is analagous to the Hammett treatment of side-chain reactions, and leads to the empirical relationship

$$\log k/k_H = \rho \sigma^+$$

where σ^+ is the substituent constant appropriate to the substituted aromatic reacting at a rate k/k_H relative to benzene, and ρ is a reaction constant. The reaction constant is a measure of the susceptibility of the reaction to changes in the substituent and the hydrocarbon structure. Consistent values of σ^+ are obtained by different methods for a wide range of substituents. Values of the reaction constant rho are given in Table II; the wide range of values can be explained as follows. As the transition

state moves further from the σ-complex in different reactions, delocalisation of the aromatic system becomes less, finally reaching the extreme case of an oriented π-complex in which little change in the aromatic system has occurred. At the same time, less stabilisation of the transition state by the substituents is evoked. Thus rho, which is a measure of this stabilisation, varies with the reaction, becoming smaller as less stabilisation is required. The rho values shown in the table, taken from Brown's compilation, demonstrate for example what has long been known, that molecular bromination is more sensitive to changes in substituent than nitration.

TABLE II[26]

Reaction	Conditions		ρ
Bromination	Br_2, AcOH, H_2O	25°	-12.1
Chlorination	Cl_2, AcOH	25°	-10.0
Acetylation	AcCl, $AlCl_3$, $C_2H_4Cl_2$	25°	-9.1
Detritiation	Various		-8.2
Bromination	HOBr, $HClO_4$, dioxan	25°	-6.2
Nitration	Various		-6.0
Mercuration	$Hg(OAc)_2$, AcOH	25°	-4.0
Ethylation	EtBr, $GaBr_3$, ArH	25°	-2.4

Brown and Stock conclude from their analysis that the transition states of aromatic substitution reactions show far less variation than do those of side-chain reactions. Olah's results do not conform to the Selectivity relationship, a fact which Olah uses to support his mechanism, and rho values for these reactions cannot be obtained in this way.

Dewar's reactivity number treatment[27,28] is essentially a theoretical derivation of a relationship similar to the Extended Selectivity treatment. Reactivity numbers are directly related to, but more simply calculated than, the localisation energies required to form the σ - complex from the hydrocarbon. Reactivity numbers show linear correlations with reactivity and variations in the slopes of the correlation lines for different reactions can be interpreted in terms of differences in transition states. This treatment has so far been successfully applied only to polycyclic aromatic compounds.

The nitrating systems.

The work of Ingold and his collaborators[29] on the mechanism of aromatic nitration established that in the majority of the systems studied the nitronium ion, NO_2^+, is the active electrophile. Many of the systems studied by these workers are extremely active nitrating media; nitric acid-sulphuric acid mixtures, for example--and at concentrations suitable for gas chromatographic product analysis lead to significant polynitration. This makes them unsuitable for this type of study. Two systems which were considered to involve NO_2^+,[10] and which on investigation proved to give smooth mononitration were nitric acid in nitromethane solvent, with added catalytic sulphuric acid, and nitric acid-acetic anhydride mixtures. In the latter system, there was doubt about the electrophile, and unusual orientation effects had also been observed (see p. 27). For this reason it was decided to compare nitrations in nitromethane with nitrations in acetic anhydride, the former solvent providing a comparison system in which reaction occurred by a well-defined kinetic route. During the course of this work the nitronium tetrafluoroborate nitrations of Olah et al.[20] were reported. These workers drew attention to the unusual behaviour of this reagent (p. 8), and a study of the product distributions from the reaction of the methybenzenes with NO_2BF_4 was therefore

undertaken. The next three sections describe the information which is available about the active nitrating species in these three systems.

Nitronium tetrafluoroborate-sulpholane mixtures.

The original intention of Olah and his co-workers in investigating nitrations using NO_2BF_4 and related salts was to examine the behaviour of an electrophilic aromatic substitution reaction in which the attacking electrophile, NO_2^+ in this case, was not formed in a pre-equilibrium step. Their pioneering work[30,31] on the preparation of the salts NO_2BF_4, NO_2PtF_6, NO_2AsF_6, and $(NO_2)_2SiF_6$ allowed these salts to be used for this work. The most useful material proved to be NO_2BF_4. Infrared examination of the solid salt[32] showed that it contains the $O{=}\overset{+}{N}{=}O$ unit. Conductivity measurements[31] in sulpholane and nitromethane supported the ionic salt structure. The overall reaction with the aromatic in sulpholane is

$$ArH + NO_2BF_4 \rightarrow ArNO_2 + HBF_4$$

The tetrafluoboric acid is stable in sulpholane, and readily removed by washing with water.

The following information about the nature of the electrophile in these solutions has been described by Olah. The attacking entity appears to be essentially non-solvated. The ortho : para ratios found for toluene[20] are higher than

values generally observed. Values for ethylbenzene, isopropylbenzene and t-butylbenzene are also slightly higher than those found in other nitrating systems.[33] Nitrations with NO_2BF_4-sulpholane mixtures display normal positional selectivity within each aromatic, but abnormally low substrate selectivity[20] (p. 8). Olah considers this to be evidence for attack by NO_2^+ without pre-equilibrium formation of this species--"free" NO_2^+ being an extremely vigorous electrophile leading to a transition state much closer to a π -complex than a σ-complex. Such π-complexes, he considers, would be expected to have similar stability over a range of substrate reactivities, leading to the observed low substrate selectivity. Heterogeneous nitration of aromatics in 1:1 sulphuric acid-nitric acid shows substrate selectivity very close to that found in NO_2BF_4 nitrations.[34] Reactions with 75% mixed acid in sulpholane and in acetic acid also show this low selectivity. Mixed acid is expected to contain NO_2^+ in high concentration, and Raman spectroscopy indicates appreciable nitronium ion concentrations in the 75% solutions.[34] 30% mixed acid in sulpholane, however, shows no detectable NO_2^+ and the substrate selectivity is similar to that found in other nitrating systems. These results are summarised in Table III.

TABLE III

Substrate selectivity in selected aromatic nitrations.[34]
Rates relative to benzene.

Substrate	Mixed acid			Nitric acid
	hetero-geneous	75% in sulpholane	30% in sulpholane	HNO_3-nitro-methane
benzene	1.0	1.0	1.0	1.0
toluene	1.24	1.60	28	26.4
o-xylene	1.02	0.90	--	--
m-xylene	0.80	1.10	> 500	--
p-xylene	1.09	1.8	> 500	22.6
mesitylene	0.68	0.33	>1000	>1000
ethylbenzene	--	1.35	24	>1000

These results were taken to indicate that nitration in "classical" nitronium ion systems in fact involves not free NO_2^+ but a weak electrophilic precursor, while in NO_2BF_4-sulpholane or in high concentrations of mixed acid the electrophile is much closer to the free nitronium ion. However, cryoscopic measurements on NO_2BF_4-sulpholane systems showed the salt to be only about 2% dissociated, and the conductivity measurements were re-interpreted in terms of conducting ion triplets.[34]

Olah concludes that $NO_2^+BF_4^-$ is the electrophile, and regards the reaction "as nucleophilic displacement by the basic aromatic hydrocarbon on the $NO_2^+BF_4^-$ ion pair (or higher associated clusters). The high energy of

activation of the π -complex results from the energy required to overcome the coulombic forces of the ion pairs."

Nitric acid-nitromethane mixtures.

Raman spectra of nitric acid in nitromethane show no trace of either the nitronium ion or the nitrate ion.[35] In solutions of nitric acid-sulphuric acid mixtures (1:1) in nitromethane, NO_2^+ is detectable down to 25% mixed acid by volume,[34] but not below this figure. Protonation of the nitromethane by nitric acid seems unlikely, since this is brought about to only a very limited extent by concentrated sulphuric acid.[36] The kinetic studies of Benford and Ingold[37] have established the following equilibria:

$$HNO_3 + HNO_3 \rightleftharpoons H_2NO_3^+ + NO_3^- \qquad \text{(fast)}$$

$$H_2NO_3^+ \rightleftharpoons NO_2^+ + H_2O \qquad \text{(slow)}$$

Reaction with aromatic then occurs:

$$ArH + NO_2^+ \rightarrow ArNO_2 + H^+$$

In accordance with this scheme, the reactions with benzene and more reactive substrates show zeroth order kinetics, reactions with halobenzenes show orders between 0 and 1, and di- and trichlorobenzenes show first order kinetics. The formation of the nitronium ion in the second step is assumed to be slow enough to be rate-determining in the reaction with activated substrates. Rates of reaction of

benzene, toluene and ethylbenzene are identical when determined separately,[37] but competitive reactions show[34] that mixed hydrocarbons compete selectively for the electrophile (benzene:toluene:ethylbenzene = 1:26:23; benzene:pxylene = 1:> 1000). These observations are in accordance with the slow formation of NO_2^+. Further, addition of NO_3^- to the reactions strongly retards the rate but induces no change from zeroth to first order kinetics. The formation of $H_2NO_3^+$ cannot therefore be rate-determining.

The rate of recombination of the nitronium ion with water must, in this reaction sequence, be much slower than the rate of reaction with aromatic. If sufficient water is added, this will compete effectively with the aromatic for the nitronium ion and the reactions should become first order in hydrocarbon. Although this change has not been observed with alkylbenzenes, Hughes et al.[38] have shown it to occur in the N-nitration of N-methyl-2,4,6-trinitroaniline, which exhibits characteristics typical of aromatic substitution. The effect of added water is the same as reducing the substrate activity--the substrate becomes less effective in competing for the nitronium ion.

The above considerations apply to solutions of nitric acid in nitromethane up to 7M. Addition of catalytic (0.01M) quantities of sulphuric acid to the system

accelerates the reaction through the equilibrium,[10]

$$H_2SO_4 + HNO_3 \rightleftharpoons H_2NO_3^+ + HSO_4^-$$

Olah has shown that high concentrations of mixed acid in both acetic acid (up to 75% mixed acid) and sulpholane contain appreciable concentrations of NO_2^+.[34] Nitrations carried out in these systems and heterogeneously in mixed acid show the almost complete lack of substrate selectivity typical of nitrations with NO_2BF_4, (Table I, p. 8), but with normal isomer distribution. (Nitromethane could not be used as a solvent for this work because the acid layer separates on addition of hydrocarbon. However, 75% mixed acid in nitromethane shows similar $[NO_2^+]$ values to sulpholane and acetic acid.) Olah also showed that water, benzene, toluene and chlorobenzene react at very similar rates with NO_2BF_4 in sulpholane.[34] On these grounds he concludes that in dilute solutions of organic solvents the nitronium ion is not the attacking electrophile, but rather some precursor is, and that NO_2^+ is formally released only when the precursor is already associated with the substrate. Olah considers that the active species is "most probably" a transition state in the formation of NO_2^+. This proposal is difficult to reconcile with the Ingold kinetics. The most likely precursor to NO_2^+ in nitromethane is the nitric acidium ion $H_2NO_3^+$, proposed by Ingold. Thus Olah's scheme would be

$$HNO_3 + HNO_3 \rightleftharpoons H_2NO_3^+ + NO_3^-$$

$$H_2NO_3^+ \overset{\text{slow}}{\rightleftharpoons} H_2O{-}{-}NO_2^+ \rightleftharpoons H_2O + NO_2^+$$

$$\downarrow ArH$$

$$Ar\text{-}NO_2 + H^+ + H_2O$$

Such a scheme agrees with the observed retardation by NO_3^-, but does not explain the effect of added water, which should increase the concentration of the reactive species and thus increase the rate.

In spite of these difficulties, there is certainly a difference between nitration with dilute solutions of nitric acid in organic solvents and nitrations in systems which might be expected to give high concentrations of either NO_2^+ or $NO_2^+BF_4^-$ ion pairs. The cause of the difference is not clear.

Nitric acid-acetic anhydride mixtures.

(a) Physical measurements.

In 1945 Vandoni and Viala[39] carried out vapour pressure measurements with nitric acid-acetic anhydride mixtures, and interpreted the results in terms of the equilibria

$$Ac_2O + 2HNO_3 \rightleftharpoons N_2O_5 + 2AcOH \quad \ldots\ldots\ldots (1)$$

$$N_2O_5 + Ac_2O \rightleftharpoons 2AcONO_2 \quad \ldots\ldots\ldots (2)$$

For mixtures with nitric acid mole fractions less than 0.5, the measurements showed that nitric acid is converted almost

entirely into acetyl nitrate:

$$Ac_2O + HNO_3 \rightleftharpoons AcONO_2 + AcOH \quad . . . . . \quad (3)$$

Raman spectra measurements[40] support this conclusion, and measurements by Jones and Thorn[41] may also be interpreted in terms of this equilibrium though the authors did not do so.[42] Freezing point measurements[43] are interpreted by Dunning and Nutt in terms of the formation of N_2O_5 and acetic acid from pre-formed acetyl nitrate. Viscosity, density and refractive index measurements by Mal'Kova[44] can be explained in terms of complete conversion of the nitric acid into acetyl nitrate for mole fractions of nitric acid up to 0.5. At higher acid concentrations, N_2O_5 is formed. Lloyd and Wyatt's vapour pressure measurements[45] agree with this conclusion. Marcus and Fresco measured the infrared spectra of nitric acid in acetic anhydride.[46] With concentrations of nitric acid up to 70 mole % no absorption by NO_2^+ could be observed. Above this concentration the absorption detected could have been due either to free NO_2^+ or to the ionic species NO_2^+-NO_3^-. On the assumption that the second possibility is correct these observations are in accord with (1) and (2) over the whole concentration range. Bordwell and Garbisch[47] studied the nitration of alkenes in nitric acid-acetic anhydride mixtures and found that if the mixture was prepared at -10° there is little evidence of reaction during mixing and little or no nitration occurs on

adding alkene at -15°. On the other hand an exothermic reaction occurs if 70% nitric acid is added to acetic anhydride at 25°, and nitration of added alkene occurs readily. Nitric acid can be recovered almost quantitatively from the mixture prepared at -10° by precipitation as urea nitrate. Addition of urea to the reaction mixture prepared at 25° gave 30-35% of the total nitric acid as urea nitrate; after one hour the precipitate formed was equivalent to 22% total acid. This work was interpreted in terms of the formation of acetyl nitrate at room temperature, this being either the effective nitrating agent or an essential precursor.

The majority of the evidence presented above favours the view that in nitric acid-acetic anhydride mixtures with mole fractions of nitric acid below 0.5, the acid is converted almost entirely into acetyl nitrate.

(b) Kinetic evidence.

Several kinetic investigations have been carried out in nitric acid-acetic anhydride mixtures. Only those which have direct bearing on the nature of the attacking species will be described. In 1935 Cohen and Wibaut[48] reported a study of the nitration of benzene in this system. The reaction was found to be third order in nitric acid and first order in benzene. Addition of urea to the reaction mixture retarded the rate of nitration and this was

interpreted as proof of catalysis by nitrous acid. The authors proposed that nitration was approximately first order in nitrous acid and second order in nitric acid. The nitrous acid concentration was assumed to depend on nitric acid, leading to the third order dependance. Nitric acid reacts with acetic anhydride to give tetranitromethane,[49] and this compound may be prepared by allowing the mixture to stand for several days. The equation is

$$4HNO_3 + 4(CH_3CO)_2O \rightarrow C(NO_2)_4 + 7CH_3COOH + CO_2$$

Cohen and Wibaut investigated this reaction and estimated the half-life of nitric acid to be about 24 hours. Studies of the nitration of benzene by nitric acid in carbon tetrachloride showed that added acetic anhydride retarded the rate. This was attributed to the more rapid formation of acetyl nitrate, which was considered a poorer nitrating agent than nitric acid.

Paul[50] followed the nitration of benzene in nitric acid-acetic anhydride mixtures at 25°, using an ultraviolet spectrophotometric method to measure the rate of nitrobenzene formation. By using an excess of nitric acid, the acid concentration was held effectively constant. The reactions showed first-order dependance on benzene, but the rate plots were curved. Paul converted them to linear plots by assuming a first-order reaction between nitric acid and acetic anhydride and choosing values of the rate of

this side reaction to give linear plots. The half-life of the side reaction estimated in this way was about one hour, very much less than the value found by direct measurement.[48] The benzene nitration was found to be second order in nitric acid, and the results were interpreted in terms of a nitronium ion mechanism;

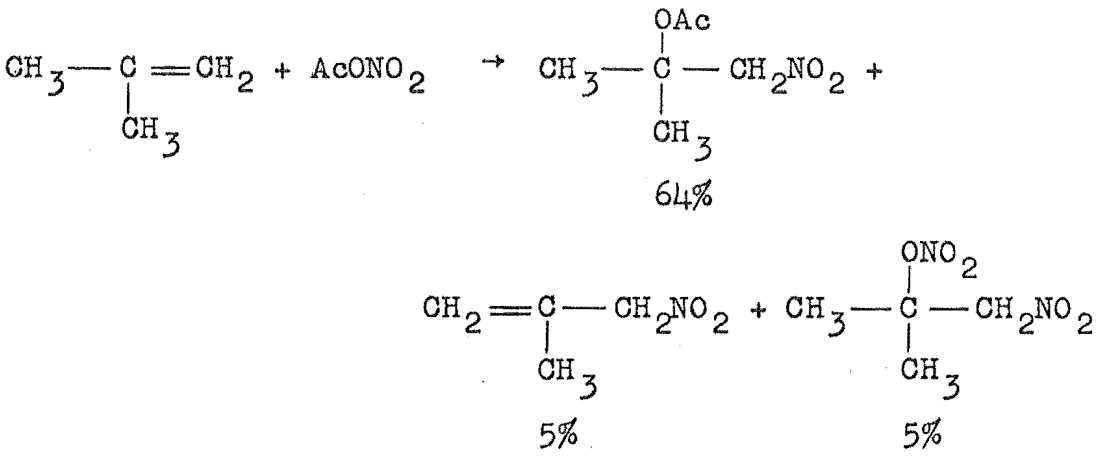
$$HNO_3 + H^+ \rightleftharpoons H_2NO_3^+$$
$$H_2NO_3^+ + Ac_2O \rightleftharpoons 2AcOH + NO_2^+$$
$$ArH + NO_2^+ \rightarrow ArNO_2 + H^+ \quad (slow)$$

This scheme requires second-order dependance on nitric acid, and accounts for the observed catalytic effect of sulphuric acid and the change to first-order nitric acid dependance in the presence of added sulphuric acid. Paul's correction for the side-reaction is, however, arbitrary and almost certainly too large. This would account for the difference between his nitric acid order and that of Cohen and Wibaut. Further, Paul's mechanism takes no account of the acetyl nitrate which is known to exist in these solutions, nor does it explain the fact noted by him and by Cohen and Wibaut, that acetic acid up to high concentrations has no effect on the rate.

The work of Bonner[51] on the conversion of 2,4-dinitrobenzyl alcohol into its nitrate ester with nitric acid-acetic anhydride mixtures in acetic acid will not be considered. Apart from the complicating presence of acetic

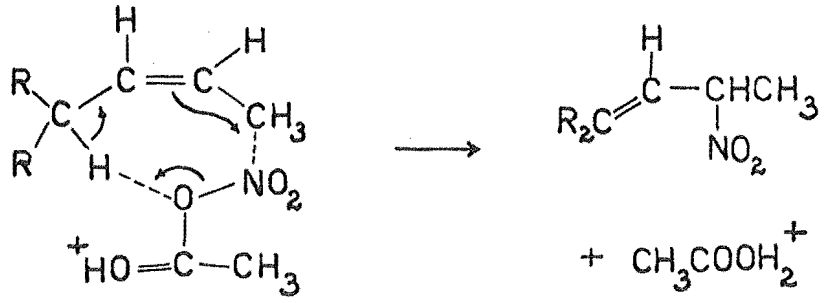
acid, good reasons for rejecting the conclusions drawn by these workers have been given by Read.[42]

Bordwell and Garbisch have studied the nitration of simple alkenes[47] and of 1,1-diarylalkenes[52] with nitric acid-acetic anhydride mixtures, and their work provides valuable information about the nature of the reactive species in these solutions. Their evidence for the formation of acetyl nitrate has already been outlined (p. 23). From the reactions of the simple alkenes the principle product is the β -nitro acetate, with smaller amounts of β -nitro alkenes and β -nitro nitrates. 2-Methylpropene serves as a typical example:



Formation of the β -nitro acetates was found to be almost entirely stereospecific and consideration of specific cases shows that acetyl nitrate or its conjugate acid is the only reasonable attacking entity which will give stereospecific addition. Further, crowded alkenes such as 2,4,4-trimethyl-2-pentene fail to give β -nitro acetates except in the

presence of added sulphuric acid. This can be explained in terms of the steric requirements of the cyclic transition state for this reaction. The formation of β -nitro alkenes from the crowded alkenes can also be explained in terms of relief of strain in the transition state:



Addition of sulphuric acid to the reactions causes marked acceleration of the rates, in support of the view that protonated acetyl nitrate is the reactive species. Acetate ions and urea both cause marked retardation, presumably by destroying $AcONO_2.H^+$ by proton abstraction. The formation of small amounts of β -nitro nitrates was believed to be due to the presence of small amounts of dinitrogen pentoxide:

$$AcONO_2 + HNO_3 \rightleftharpoons AcONO_2.H^+.NO_3^-$$

$$AcONO_2H^+NO_3^- \rightleftharpoons N_2O_5 + AcOH$$

This accounts for the increased yields of β -nitro nitrates with added lithium nitrate and for the decreased yields in added sulphuric acid. Studies of the nitration of

1,1-diaryl alkenes support the observation of the strong catalysis by sulphuric acid. In alkenes such as 1,1-diphenyl propene, in which attack at the double bond is likely to be sterically hindered, N_2O_5 assumes a significant role and good yields of β-nitro nitrates are obtained.

From the evidence summarised above it seems likely that the important nitrating species in nitric acid-acetic anhydride mixtures are protonated acetyl nitrate and to a lesser extent dinitrogen pentoxide and acetyl nitrate.

(c) Evidence from ortho:para ratios.

A problem related to studies in nitric acid-acetic anhydride mixtures is the high ortho:para ratios sometimes observed for nitrations in this system. These ratios, which are high compared with values obtained for the same substrate in other nitrating systems, have been observed for anisole, acetanilide and methyl phenethyl ether, and are summarised in Table IV.

TABLE IV

A Ortho:para ratios from the nitration of anisole and acetanilide.[10]

Substrate	Nitrating medium	ortho:para ratio
anisole	HNO_3 in H_2SO_4	0.46
	HNO_3 (d = 1.42)	0.69
	HNO_3 in AcOH	0.81
	HNO_3 in Ac_2O	2.54
	$PhCO.ONO_2$ in MeCN	3.00
acetanilide	HNO_3 in H_2SO_4	0.25
	HNO_3 (99%)	0.31
	HNO_3 in Ac_2O	2.28

B Ortho:para and meta:para ratios from nitration of methyl phenethyl ether.[53]

Nitrating medium	ortho:para ratio	meta:para ratio
HNO_3	0.76	0.12
HNO_3 in Ac_2O	1.84	0.11
$AcONO_2$ in MeCN	2.22	0.14

It is generally acknowledged that other substrates with nitric acid-acetic anhydride mixtures give ortho:para ratios similar to those obtained from reaction with nitric acid, mixed acid, and nitric acid-acetic acid mixtures (Table V), although Topchiev[54] has reported high ortho:para ratios for nitrations of toluene, phenol and benzyl chloride with acetyl nitrate in an unspecified solvent.

TABLE V

Ortho:para ratios from nitration of toluene and t-butylbenzene

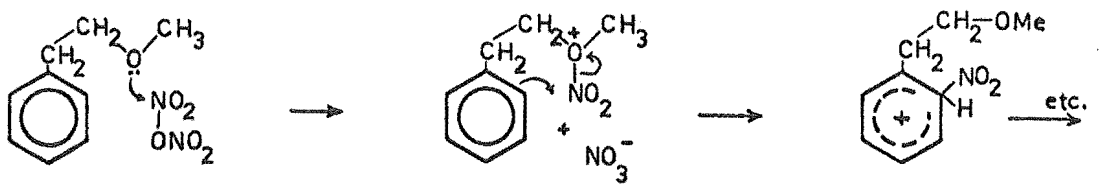
Substrate	Nitrating medium	ortho:para ratio	References
toluene	HNO_3 in H_2SO_4	1.58	55, 56
	HNO_3 in Ac_2O	1.87	57, 58, 59
	HNO_3 in $MeNO_2$	1.70	57, 58
	HNO_3 in 90% AcOH	1.41	60
t-butylbenzene	HNO_3 in H_2SO_4	0.22	55
	HNO_3 in Ac_2O	0.13	57, 59
	HNO_3 in $MeNO_2$	0.15	57
	HNO_3 in 90% AcOH	0.15	60

The nitration of biphenyl in nitric acid-acetic anhydride mixtures has been considered to give high ortho:para ratios.[61-63] Recent work has shown, however, that the "anomalous" ratio occurs in mixed acid nitration of biphenyl[63] and this has been attributed to the heterogeneous

reaction. High activation of the ortho position in biphenyl occurs in other reactions[64] and can be explained in terms of the planar configuration of the two rings in the ortho transition state. Further, the results of reference 61 have been utilised by Brown et al.[65] and show good fit with other results on selectivity plots for biphenyl. There remain therefore the high ortho:para ratios for anisole, acetanilide and methyl phenethyl ether, if Topchiev's results are ignored for want of detailed information. Three explanations have been put forward for these.

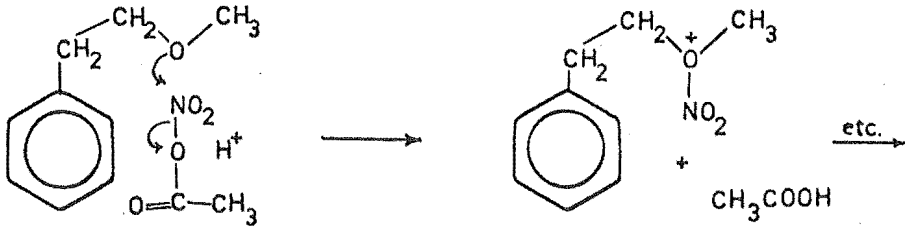
Paul[66] has proposed that the high percentage of ortho product from nitration in acetic anhydride arises from the greater electrostatic effect of the substrate dipole moment in a medium of low dielectric constant (20.7 for acetic anhydride). This view is rejected by Norman and Radda[53] on the grounds that product ratios in acetic acid (dielectric constant 6.4) are the same as those from nitric acid and also from mixed acid (dielectric constant about 50). The other two explanations are complementary. De la Mare[10] proposes that the change arises entirely from a change in nitrating species in acetic anhydride, but it seems unlikely that such a large change could arise solely from a change in the electrophile. The experimental meta values are not sufficiently accurate to allow meaningful comparison of the selectivity factors for the various

solvents, and in his examination of the reactions of anisole, Brown did not examine nitration data for fit to the selectivity relationship. Thus this postulate cannot be tested. A second, related explanation, offered by Norman and Radda,[53] seems most satisfactory. These workers examined the behaviour of methyl phenethyl ether and showed that the ortho:para ratio was higher for nitric acid-acetic anhydride and acetyl nitrate-acetonitrile than for other systems, (Table IVB), but that the meta:para ratios were essentially unchanged. This shows that the high ortho:para ratio does not arise from protonation of the oxygen, since such protonation would result in greater deactivation of the para than the meta position. The explanation offered is that in addition to "normal" nitration by NO_2^+, nitration by N_2O_5 also occurs. Paul's work is cited as evidence for nitronium ion nitration. N_2O_5 is attacked by an S_N2 displacement of nitrate ion thus:



This mechanism is also applicable to anisole and acetanilide.

Although the explanation is offered in terms of dinitrogen pentoxide, the same reasoning can be applied to protonated acetyl nitrate, with this species responsible for all the nitration reaction, and enhanced ortho activity arising from a cyclic transition state.

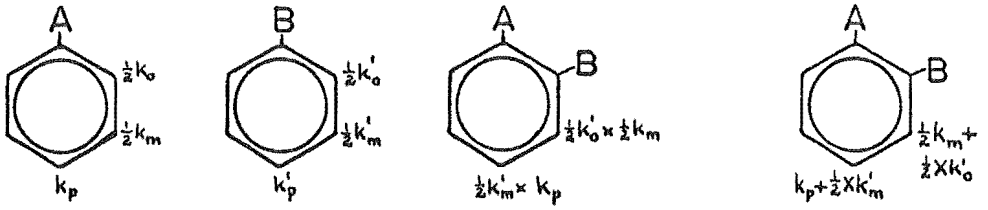


Such a scheme would require an acetic acid leaving group, which might be expected to be more effective in acetic anhydride than NO_3^-.

It is concluded from this survey that the most important attacking species in nitric acid-acetic anhydride mixtures is protonated acetyl nitrate.

Additivity in Electrophilic Aromatic Substitution

The first attempt to predict the effect of more than one substituent on the reactivity of the aromatic nucleus was made by Holleman in 1924.[67] On the basis of the experimental information available, Holleman proposed two methods of calculating isomer distributions in poly-substituted benzenes. Both methods assumed that the groups on the benzene ring activated the ring independently, the influence of each group at the available ring positions being measured by the product distribution of the relevant monosubstituted benzene. The two methods are illustrated below:



Total Relative Rate: 1 × "Product rule" "Sum rule"

The relative rates of substitution for the two mono-substituted compounds at each ring position allow calculation of similar quantities for the di-substituted compounds by either the "sum" or the "product" rule. From these values the isomer distributions for the disubstituted compounds could be calculated. Holleman was aware of the

importance of the relative rates of overall substitution of the two parent compounds and corrected for this factor in his "sum" rule but not in the "product" rule. The experimental information available did not allow a decision between the two methods to be made, but Holleman notes[67] that both methods give the correct qualitative result in almost all of the large number of cases he cites. De la Mare[10] has summarised the early experimental evidence for disubstituted benzenes; examination of this work shows that most workers assumed some form of "sum" relationship and obtained rough qualitative agreement between predicted and experimental results.[68,69]

An important contribution towards an understanding of the effects of two or more substituents was made by Scheffer[70] and independently by Bradfield and Jones,[72] who interpreted Holleman's data in terms of the Arrhenius equation. Scheffer showed that the relative rates of nitration in disubstituted benzenes could be deduced from the rates of nitration of monosubstituted benzenes provided the entropy of activation at each position in the benzene ring is the same. Bradfield and Jones[72] and Jones et al.[73-75] examined the nuclear chlorination and bromination of over two hundred aromatic ethers of the type $\underline{p}$-RO-C_6H_4-X and RO-$C_6H_3X_2$ and showed that the entropy of activation was constant, that the changes in rate observed arose from

changes in the activation energies, and that the value of E_a is determined by the sum of characteristic contributions from the substituents on the ring. Work by Stubbs and Hinshelwood[76] and others, on activation energies of side-chain reactions, including the dissociation of substituted benzoic acids[77] also showed constant entropies of activation for any given reaction, and characteristic additive contributions to the energy of activation by different substituents.

This concept of a characteristic contribution to the energy of activation made by any given substituent is the basis of the very successful treatment developed by Hammett[78] for side-chain reactions of disubstituted benzenes. Hammett's treatment, and other such "linear free energy relationships" express this concept in much more useful terms, allowing simple evaluation of the substituent's effect on the activation energy without calculation of the activation energy change itself. This treatment has been extended by Jaffé[79] and others to side-chain reactions of polysubstituted benzenes, by assuming that these characteristic contributions of each substituent are additive; this postulate is the "Additivity Principle." It has been successful in predicting side-chain reactivities in a wide variety of reactions. Thus, the Hammett equation for one substituent (other than the reacting side-chain) is

$$\log k' = \rho \sigma$$

where k' is the reaction rate for the substituted compound relative to the unsubstituted compound, ρ is the reaction constant (which includes the temperature-dependent entropy term of the Arrhenius equation) and σ is the characteristic contribution of the substituent. The Additivity Relationship gives, for a benzene nucleus with i non-reacting substituents,

$$\log k' = \rho \sum_i \sigma_i$$

Application of this approach to electrophilic aromatic substitution has been much less rapid. Condon[80] was the first to show that a linear free energy relationship could successfully predict aromatic reactivity. In such systems, the unsubstituted reference compound is benzene, and the rate of substitution at any given position in the substituted compound relative to one position in benzene is termed the "partial rate factor" or "partial relative rate" for that position, k_f. The Additivity Principle gives the expression for the partial rate factor as

$$\log k_f = \rho \sum_i \sigma_i \qquad \text{or} \qquad k_f = 10^{\rho \sum_i \sigma_i}$$

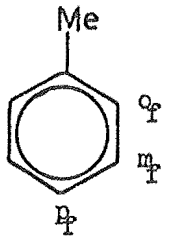
(σ_i is now a constant characteristic of the influence of each substituent at a given position in the ring, rather than at a side-chain reaction site). The total reaction rate k_t for the substituted aromatic relative to one

position in benzene is the sum of the partial rate factors for each position, thus[150]

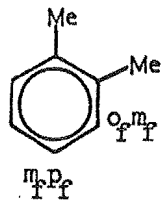
$$k_t = \sum_f k_f = \sum_f 10^{\rho \sum_i \sigma_i}$$

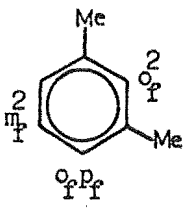
which may be written as $k_t = \sum_f \prod_i k_i$.

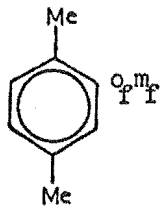
Condon's calculations illustrate the use of this equation. If the partial rate factors for the halogenation of toluene are o_f, m_f, and p_f as shown (determined from the isomer distribution and the relative rates of halogenation of toluene and benzene)



then the partial rate factors for the free positions in o-, m-, and p-xylene, together with the total rates of substitution are:







Total rate k_t: (benzene=6)	$2o_f m_f + 2m_f p_f$	$o_f^2 + 2o_f p_f + m_f^2$	$4o_f m_f$

(Total rates relative to benzene=1 are given by $k_t/6$.)

This treatment is effectively the same as Holleman's original "Product rule" with allowance made for the relative rates of reaction of the parent aromatics. All the methods discussed are based on the general concept of additive contributions to the free energy of activation by substituents in the ring; Condon's method is particularly convenient for the methylbenzenes.

Condon uses the rate data of de la Mare and Robertson[81] for chlorination and bromination of polymethylbenzenes in 99% acetic acid (some values are for chlorination and some for bromination), and the isomer distribution figures for toluene derived from Wertyporoch's work[82] on $SbCl_5$-catalysed chlorination. Since all three reactions are now known to give quite different values for partial rate factors,[83] and since Condon was forced to assume a value for the meta partial rate factor, the agreement found by Condon between experimental and calculated results is remarkably good. (Table VI)

TABLE VI

Relative rates of halogenation of polymethylbenzenes (benzene=1)

	p-xylene	o-xylene	m-xylene	mesitylene	pentamethylbenzene
Calculated	2.0×10^3	2.5×10^3	2.4×10^5	1.6×10^8	13×10^8
Experimental	2.2×10^3	4.6×10^3	4.3×10^5	1.8×10^8	7.8×10^8

In a second paper,[84] Condon extends this treatment to the basicities of the polymethylbenzenes. Basicities determined by McCaulay and Lien,[85] and McCaulay, Shoemaker and Lien[86] for durene, isodurene, prehnitene and pentamethylbenzene were used to calculate "partial relative basicities" for ortho-, meta-, and para- methyl groups, analagous to partial rate factors for substitution reactions. These values were used to calculate basicities for the other methylbenzenes, with good agreement between calculated and experimental values. (Table VII)

TABLE VII

Relative basicities of polymethylbenzenes (m-xylene=1)

	Calculated	Observed
Toluene	0.012	0.001
p-xylene	0.042	0.05
o-xylene	0.05	0.10
m-xylene	1.3	1.0
pseudocumene	2.6	2.0
hemimellitene	6.6	6.7

Condon also found good correlation between the basicities and rates of halogenation, the points showing excellent fit to the line

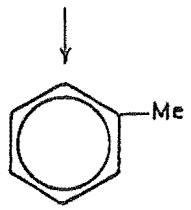
$$\log(\text{relative rate}) = 1.27\log(\text{relative basicity}) + \text{constant.}$$

Noting that this relationship corresponds exactly to the Hammett equation $\log k/k_o = \rho \sigma$ Condon calculated values of ρ for the halogenations and the reaction with $HF.BF_3$ (basicity).

	ρ calculated from $\sigma_{p\text{-Me}}$	from $\sigma_{m\text{-Me}}$
Halogenation	-17.3	-10.1
Basicity	-12.7	-7.1

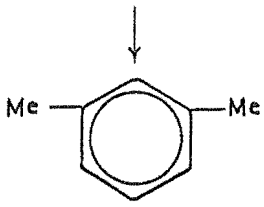
His comment that the large differences between the values of ρ calculated from the two σ values "suggests that side-chain σ values may need modification in order to correlate aromatic ring carbon reactivity" foreshadows the work of Brown et al.[87] in deriving such modified values.

In 1955 Brown and McGary[88] applied Condon's treatment to the mercuration reaction, determining the product distribution for toluene and the reaction rates for the polymethylbenzenes under identical conditions. Experimental difficulties in determining the amount of ortho-isomer formed in the mercuration of toluene led these workers to calculate the value of the ortho partial rate factor from the rates of reaction of the polymethylbenzenes. They found that no single value would give satisfactory agreement for all the hydrocarbons, and suggested that the large steric requirements of the mercuration reaction required the use of "single" and "double" ortho partial rate factors, thus:



'single' ortho

$o_f = 5{\cdot}45$



'double' ortho

$o_f = 4{\cdot}8$

Use of these two values in calculating relative reactivities reduced the standard deviation of the calculated from the observed values from 12% to 6% (Table VIII).
Marino and Brown[89] determined the relative rates and isomer distributions from acetylation of methylbenzenes by acetyl chloride--$AlCl_3$ in ethylene dichloride solution, a reaction with very large steric requirements. These results, summarised in Tables VIII and VIIIA, show much larger differences between observed and calculated results than found for mercuration. The isomer distributions in Table VIIIA show poor agreement between observed and calculated values--it is interesting to note that while the calculated overall rate for hemimellitene is the same as the observed rate, the calculated isomer distribution is seriously in error. Later work by Brown et al. is summarised in Table IX. The calculated results for the halogenation reactions are obtained using mean values for the meta partial rate factor in toluene, which is difficult to determine experimentally.

TABLE VIII

Relative rates of mercuration and acetylation of methylbenzenes

Hydrocarbon	Mercuration[88]		Acetylation[89]	
	Obs.	Calc.	Obs.	Calc.
benzene	1.0	1.0	1.0	1.0
toluene	5.0	5.3	128	128
o-xylene	16.0	14.7	2130	1200
m-xylene	34.5	35.0	347	1130
p-xylene	8.2	7.2	23.5	14.4
mesitylene	209	194	2920	7580
hemimellitene	68	71.5	8260	8240
pseudocumene	49	41.5	1760	2720
durene	30	30.4	102	156
isodurene	257	255	7430	24200
prehnitene	126	121	7300	25800
pentamethylbenzene	224	255	13200	58000

TABLE VIII A [89]

Product distribution from acetylation of methylbenzenes

Hydrocarbon	isomer	Observed	Calculated
m-xylene	2-	0	0.3
	4-	97.5	99.4
	5-	2.5	0.3
hemimellitene	4-	21.0	65.2
	5-	79.0	34.8

Relative rates of electrophilic attack on polymethylbenzenes (benzene = 1)

Hydrocarbon	Relative Rates							
	Bromination[83]		Chlorination[83]		Benzoylation[a,90]		Benzoylation[b,90]	
	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
benzene	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
toluene	605	605	344	344	117	117	110	110
o-xylene	5.32×10^{3}	5.54×10^{3}	2.1×10^{3}	2.37×10^{3}	1076	1393	993	1120
m-xylene	5.14×10^{5}	5.44×10^{5}	1.85×10^{5}	2.32×10^{5}	698	396	619	396
p-xylene	2.52×10^{3}	2.20×10^{3}	2.08×10^{3}	2.04×10^{3}	106	243	99	140
hemimellitene	1.67×10^{6}	2.67×10^{6}						
pseudocumene	1.52×10^{6}	1.66×10^{6}						
mesitylene	1.89×10^{8}	4.36×10^{8}						
prehnitene	1.10×10^{7}	1.46×10^{7}						
isodurene	0.42×10^{9}	1.60×10^{9}						
durene	2.83×10^{6}	3.63×10^{6}						
pentamethyl-benzene	0.81×10^{9}	4.39×10^{9}						

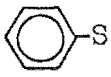
[a] In ethylene dichloride solvent. [b] In benzoyl chloride solvent.

The mean is obtained from the experimental value and values obtained by calculation assuming the Additivity Principle to be valid. The agreement between observed and calculated rates over such large variations in reactivity is very good indeed for the chlorination and bromination reactions.

Reactions involving displacement of groups other than hydrogen from the aromatic nucleus also provide support for the validity of the Additivity Principle. These reactions have been shown comparable in all respects to conventional aromatic substitution.[91] They provide a powerful test of the principle since the partial rate factor at a given position in the ring, rather than the total rate of reaction, is determined for the compound studied. Benkeser et al. measured rates of protodesilylation[92] and of mercuridesilylation,[93] and Eaborn and Moore[94] the rates of protodesilylation of polymethylbenzenes. All have found generally good agreement between observed rates and values calculated from toluene partial rate factors. The results are summarised in Table X. The calculated rates of mercuridesilylation in Table X have been obtained from Benkeser's values for the monomethyl compounds.

TABLE X

Relative Rates of Protodesilylation and Mercuridesilylation of Methyl-substituted phenyltrimethylsilanes

Hydrocarbon (R=$SiMe_3$)	Relative Rates ( =1)					
	Proto-desilylation[a]		Proto-desilylation[b]		Mercuri-desilylation	
	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
R-benzene	1.00	--	1.00	--	1.00	--
o-R-toluene	15.7	--	18.3	--	11.3	--
m-R-toluene	2.19	--	2.38	--	2.59	--
p-R-toluene	14.3	--	22.8	--	10.7	--
2-R-p-xylene	34.8	34.4	42.9	43.6	24.3	29.3
4-R-m-xylene	277	225	422	417	~160	121
2-R-m-xylene	3380	246	3530	335	too fast to measure	
4-R-o-xylene	33.6	31.3	56.1	54.3	27.2	27.7
3-R-o-xylene	94	34.4	71.9	43.6	43.0	29.3
5-R-m-xylene	--	--	6.0	5.7	--	--
R-mesitylene	--	--	53,000	7640	--	--

[a] Cleavage in glacial acetic acid-HCl[27]

[b] Cleavage in aqueous methanol-$HClO_4$[29]

Steric interaction between methyl groups and the leaving group in these reactions should accelerate the reaction; this effect is clearly occurring in 2-R-m-xylene, 3-R-o-xylene and R-mesitylene. Lauer et al.[95] have shown the protodedeuteration of benzene and the monoalkylbenzenes to be a typical electrophilic substitution reaction. Extension of this work to polymethylbenzenes[96] gives results which agree well with the rates calculated from partial rate factors for toluene and correlate well with observed basicities. Table XI summarises the rate data.

TABLE XI

Relative rates of protodedeuteration of polymethylbenzenes

	Observed	Calculated
benzene	6	6
toluene	934	934
p-xylene	5.1×10^{3}	3.8×10^{3}
o-xylene	6.2×10^{3}	5.1×10^{3}
m-xylene	1.8×10^{5}	2.8×10^{5}
pseudocumene	5.1×10^{5}	6.5×10^{5}
hemimellitene	6.6×10^{5}	8.1×10^{5}
durene	1.7×10^{6}	1.9×10^{6}
mesitylene	5.7×10^{7}	8.1×10^{7}
isodurene	1.5×10^{8}	2.0×10^{8}
pentamethylbenzene	1.6×10^{8}	3.9×10^{8}

The differences between the observed and calculated results, which are larger than those found by Brown for mercuration, must arise in part from uncertainty in Lauer's value for m_f. However, while calculation of o_f, m_f, and p_f from the experimental rates for o, m-, and p-xylene gives values appreciably different from those determined directly from toluene (o_f=218.7, m_f=5.8, p_f=311.3; values used by Lauer from toluene: o_f=250, m_f=3.8, p_f=420), rates calculated from these values are no closer to the experimental rates than Lauer's values.

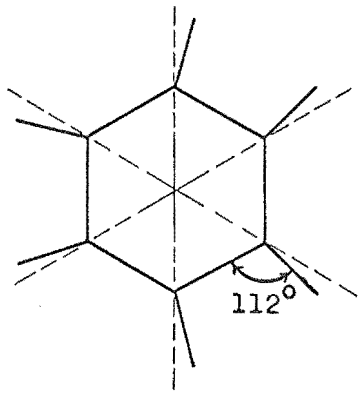
The foregoing discussion has been limited to the methyl benzenes. Extension of the Additivity Principle to different substituents, and to variously-substituted benzene compounds is straightforward, but little experimental evidence is available to allow this application to be tested. Some work on the Selectivity Relationship (for example, references 97, 98 and 99) gives information for MeO- and Bu^t- groups, but in every case the large uncertainty in the value of m_f makes the results of limited value. Stock and Baker[99] conclude that the Additivity Principle may be less satisfactory for substituents other than methyl than it is for the methyl group. As this thesis is concerned only with methyl substituents, the application of additivity to other substituents will not be considered further.

The experimental results for the polymethylbenzenes

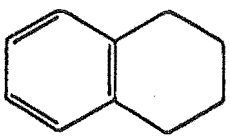
discussed shows that the Additivity Principle is capable of successfully predicting rates of substitution in the reactions studied, generally to within a factor of two in rates of the order of 10^6. Deviations between observed and calculated results are generally random, and the only systematic variations which have been noted are those resulting from buttressing effects in the mercuration and the protodesilylation reactions. The use of the Additivity Principle to calculate isomer distributions has been tested only with the acetylation reaction, which has very large steric requirements. No recent work has been reported on the application of the Additivity Principle to nitration of methylbenzenes, and as nitration is one of the most intensively studied aromatic substitution reactions, product distributions resulting from the nitration of all the methylbenzenes giving more than one isomer have been determined and compared with values calculated from the results for toluene.

The Mills-Nixon Effect

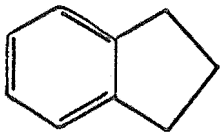
In 1930 Mills and Nixon[100] proposed the structure for benzene shown below.



In attempting to find experimental evidence to support this structure they examined the two fused-ring compounds indan and tetralin. By making reasonable assumptions about the geometry of the five- and six-membered alicyclic rings, and examining the angle deformations required to fuse these across the benzene ring, structures I and II were shown to be the more stable of the two canonical forms possible for each hydrocarbon.



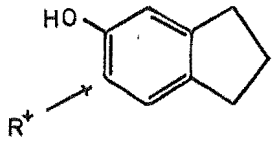
I
Tetralin



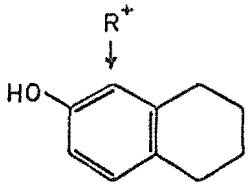
II
Indan

Mills and Nixon considered that the aromatic bonds would be effectively fixed in the configurations shown by the higher

stability of these two forms. To test this, the bromination and diazo-coupling of 5-indanol(III) and 6-tetralol(IV) were studied, in the belief that like aliphatic enol systems, attack in the phenols would occur at the double bond carrying the hydroxyl group.



III



IV

The results were in accord with prediction, substitution occurring almost entirely at the positions shown.

Following this initial paper much experimental work appeared in the literature dealing with the possibility of bond fixation in indan and tetralin. This has been reviewed by Remick[101] and by Huckel.[102] Oxidation potentials,[103] chelation studies[104] and dipole moments[105] of substituted hydrocarbons gave conflicting results, as did reactivity studies.[106,107] Kistiakowsky[108] concluded from heats of hydrogenation studies that no significant loss of aromatic resonance energy occurs in either indan or tetralin. Recent NMR studies of long-range spin-spin coupling in methylindans and tetralins[109] have shown that the common bond in indan has a slightly higher electron density than a normal aromatic C-C bond, rather than the lower value of the Mills-Nixon configuration. Ozonolysis

studies of methylindans and tetralins are reported to demonstrate slight bond localisation in the opposite configuration to that of Mills and Nixon.[110]

Several quantum mechanical treatments of the Mills-Nixon effect have been reported. The earliest of these, by Sutton and Pauling in 1935[111] makes assumptions about bond angles in ethylene which are no longer tenable. Wheland[112] makes brief comment on 5-indanol. In 1946, Longuet-Higgins and Coulson[113] showed from molecular orbital calculations that the common bond in indan is shorter than an aromatic C-C bond. Berthier and Pullman[114] published carbon free valence indices and bond orders calculated using arbitrary exchange integrals to allow for hyperconjugative release by the methylene groups to the benzene ring. The bond orders indicate a higher double-bond character for the common bond in indan than in tetralin, and the free valence indices of the ar- β carbon atoms are higher than those of the ar- α carbon atoms. The free valence indices calculated for 5-indanol and 6-tetralol are in the order required to explain the substitution observed by Mills and Nixon, but the differences involved are extremely small.

Since it seems certain that any bond localisation in the aromatic systems of indan and tetralin will be small, electrophilic attack on the aromatic nucleus in these compounds must be considered to proceed by the usual mechanism. The favoured position of substitution (for

irreversible attack) will be that giving the most stable transition state. The ground state configuration of the molecule is of no consequence, since each transition state arises from the same ground state. Failure to appreciate this point has led to confusion in discussions of the Mills Nixon effect in the literature, and the use, following the original paper, of reactivity studies as evidence for or against the Mills-Nixon configuration. Such studies can give no information about the nature of the ground state bonding provided the aromatic system is not too seriously distorted. However, the results of Mills and Nixon require explanation, and the effect of the fused five- and six-membered alicyclic rings on the behaviour of the benzene ring towards electrophilic attack is a necessary basis for any explanation. Examination of the literature shows that little reliable information is available. The work of Mills and Nixon,[100] and of Schroeter,[115] on the hydroxy-derivatives has recently been confirmed by Pascual,[116] and Granger et al.[117] have studied Friedel-Crafts cyclisation of indan- and tetralin-3-propionyl chlorides. Studies of the reactivity of the unsubstituted hydrocarbons up to 1960 have been reviewed by Berthier and Pullman[114] and Table XII summarises this information. Since this review, Granger et al.[118] have reported chloromethylation, and Tanida and Muneyuki[119] nitration of indan and tetralin. (Table XII) The results reviewed by Berthier and Pullman are insufficiently accurate

to be useful, and refer to reactions which are likely to be reversible or to involve very bulky attacking entities.

TABLE XII

Substitution reactions of indan and tetralin

Reagent	Position of Substitution		Ref.
	Indan	Tetralin	
Cl_2	--	66% β, 34% α	114
Br_2		75% β, 25% α	114
H_2SO_4	β	β +small α	114
$CO/HCl+CuCl_2/AlCl_3$	β+others*	--	114
$C_2H_5Br/AlCl_3$	--	β *	114
$CH_3Br/AlCl_3$	--	β +others*	114
$SO_3HCl/CH_3Cl-(NH_4)_2CO_3$	70% β*	--	114
$HCN/HCl/AlCl_3$	45% β *	--	114
Succinnic anhydride/ $AlCl_3$	β *	β *	114
$CH_3OCH_2Cl/AcOH$	--	90% β, 10% α	114
dimethyl- β,β-acrylic acid/$AlCl_3$	--	70% β*	114
$CH_3COCl/AlCl_3$	β *	β *	114
HNO_3-$MeNO_2$	50% β, 50% α	51.6% β,48.4% α	119
CH_2O/HCl	80% β, 10% α	75% β, 25% α	118

* Other products not specified.

The lack of accurate product analyses from electrophilic substitution reactions of indan and tetralin made the study of the nitration of these two hydrocarbons of interest, and product distributions were determined in the three nitrating systems used.

EXPERIMENTAL

Melting points were determined on an "Electrothermal" electrically heated melting point apparatus and are not corrected. Boiling points are at 760mm pressure unless otherwise stated. Infrared spectra were obtained on a Perkin Elmer model 137 "Infracord" using sodium chloride plates. Nuclear magnetic resonance spectra were run on a Varian A60 machine. Liquid phases for gas chromatography were specially-prepared commercial materials.

Preparation and Purification of Materials

(á) Hydrocarbons

The purity of the hydrocarbons used for analyses was checked by comparison of the infrared spectra with standard spectra of the American Petroleum Institute collection, and by gas chromatography. Each hydrocarbon was analysed on both an Apiezon "L" and a tricresyl phosphate column on the Pye Argon chromatograph.

Toluene (Riedel de Haen "fur Analyse") was dried over phosphorus pentoxide and distilled. It had b.p. 110-111°/ 758mm (lit.[121] 110°), and showed no impurities on the gas chromatograph.

o-Xylene (L.Light and Co.) was purified by Clarke and Taylor's sulphonation method.[120] Recrystallisation of the

sodium sulphonate followed by steam distillation of the acid gave a product which boiled at 66°/57mm (lit.[121] 50°/35mm), and showed no impurities on the gas chromatograph.

m-Xylene (B.D.H. Laboratory Reagent) was dried by passing down a column of Linde 4A Molecular Sieve, and distilled. The product (b.p. 139-140°/758mm, lit.[121] 139.3°) showed no impurity on the gas chromatograph under conditions which separated the three xylene isomers.

Hemimellitene (Halewood Chemicals 98%) was used for all reactions without purification. A small quantity of this material purified on the Megachrom to better than 99.5% gave product distributions identical with those obtained from the commercial material.

Pseudocumene (L.Light and Co.) was dried by passing down a column of Linde 4A Molecular Sieve. Distillation gave a product, b.p. 167-168°/760mm (lit.[121] 168-169°), which showed less than 1% impurity on the gas chromatograph.

Tetralin (Fluka 99.9%) was dried by passing down a column of Linde 4A Molecular Sieve. The fraction b.p. 203-204°/756mm (lit.[121] 207.3°) showed no impurity on the gas chromatograph, and was used for all reactions.

Indan (Matheson, Coleman and Bell, Reagent grade) was used without purification. It had b.p. 176-177°/760mm (lit.[121] 177°), and showed no impurity on the gas chromatograph.

(b) Reagents and Solvents

Acetic Anhydride (B.D.H AnalaR) was stored for six days over sodium, then refluxed under vacuum for four hours. Fractional distillation under reduced pressure gave a major fraction, b.p. 43-44°/15mm (lit.[121] 44°/15mm), which was retained for use. This fraction showed no trace of the peak at about δ =5.8p.p.m. in the NMR spectrum, arising from the acetic acid-OH proton. (δ from T.M.S.)

Nitromethane(Matheson, Coleman and Bell) was dried by passing down a column of Linde 4A Molecular Sieve. Distillation gave a major fraction, b.p. 101-101.5°/760mm (lit.[121] 101-101.5°), which was retained for use. This was the only satisfactory method found for drying nitromethane. Other methods gave a solvent which formed a two-phase system on addition of the small quantities of sulphuric acid required for the reactions.

Sulpholane(Light's Reagent grade) was dried by passing down a column of Linde 4A Molecular Sieve. Distillation gave a product, b.p. 152°/10mm which solidified at room temperature.

Nitric Acid was prepared by distillation of a mixture of one volume fuming nitric acid (d=1.52) and two volumes 98% sulphuric acid at room temperature and 2mm pressure. The product, collected in a dry ice trap, was colourless and

could be stored in dry ice indefinitely. The second distillation carried out by Benford and Ingold[37] was unnecessary provided distillation was carried out below 35°. Read[42] has shown that the acid obtained by this method contains less than 0.005mole percent of nitrite and gives an acid titre of 99.8±0.3%.

Nitronium tetrafluoroborate was prepared from nitric acid and anhydrous hydrogen fluoride (I.C.I.) by the method of Kuhn and Olah.[30] The final product after washing with "Arcton 113" (I.C.I.Ltd.) was a white solid which could be stored indefinitely over phosphorus pentoxide. The boron trifluoride required for this preparation was made from KBF_4, B_2O_3 and concentrated sulphuric acid as described by Booth and Willson.[122]

Diacetyl peroxide was prepared by Slagle and Shine's method[123] as a white crystalline solid. No check on purity was made.

Hydrogen peroxide 95-100% was prepared by distillation of 130 vols. hydrogen peroxide solution (with a trace of sodium pyrophosphate as stabiliser) under vacuum from an oil bath at 60-65°.[124] The fractions used were those boiling at 48-50°/14mm and 50-54°/14mm (lit.[124] for 90-100% 40-45°/10mm).

(c) Reaction Products

The compounds whose preparation is described in this section were all shown to give one peak on the Pye Argon gas chromatograph except where otherwise stated. Where likely side products from the preparation were available, columns were chosen which could resolve these impurities from the main product. Phenyl acetates frequently contain starting material when prepared from the phenol. Infrared analysis and gas chromatography showed the products to be free of phenol except in the cases mentioned.

o-Nitrotoluene and m-nitrotoluene were commercial materials redistilled.

p-Nitrotoluene(Hopkin and Williams "Purified" grade) was recrystallised from methanol and showed less than 1% of the other isomers on the gas chromatograph. It had m.p. 54° (lit.[121] 54.5°).

p-Cresyl acetate was prepared from redistilled p-cresol by treatment with sodium hydroxide and acetic anhydride.[125] Distillation of the crude product gave an oil, b.p. 210-211° (lit.[121] 212-213°).

3-Nitro-o-xylene (L.Light and Co.) was distilled. It had b.p. 96-97°/5mm (lit.[121] 131°/20mm).

4-Nitro-o-xylene (L.Light and Co.) was recrystallised three times from ethanol. It had m.p. 29.5-30° (lit.[121] 30°).

3,4-Dimethylphenol was prepared from purified 4-nitro-o-xylene by reduction to the amine followed by diazotisation and hydrolysis of the 3,4-dimethylanilinium sulphate in 50% sulphuric acid. Standard methods were used in each step. The product, obtained in 15% yield, crystallised in two forms from 50-70° petroleum ether; needles with m.p. 62.5° (lit.[121] 62.5°) and granules with m.p. 65° (lit.[121] 65°).

3,4-Dimethylphenyl acetate was prepared from the phenol by treatment with sodium hydroxide and acetic anhydride.[125] Distillation of the crude product gave an oil, b.p. 240-242° (lit.[126] 241°), crystallising at about 15°.

2,3-Dimethylphenyl acetate was prepared from commercial 2,3-xylenol by the method used for the 3,4-isomer. The product had b.p. 222-224° (lit.[126] 226-228°).

2-Nitro-m-xylene was prepared in 68% yield from commercial m-2-xylidine by peracetic acid oxidation as described for 5-nitroindan. The product had b.p. 115-117°/4mm.

4-Nitro-m-xylene (Fluka "purum") was used after one distillation. It had b.p. 120°/4mm.

2,4-Dimethylphenyl acetate was prepared from commercial 2,4-dimethylphenol (m.p. 28°, lit.[121] 27-28°) by treatment with sodium acetate and acetic anhydride.[127] The

product was a colourless liquid, b.p. 88-89°/2mm (lit.[121] 108°/13mm).

2,6-Dimethylphenyl acetate was prepared from commercial 2,6-dimethylphenol (m.p. 49°, lit.[121] 49°), by the method used for the 2,4-isomer. The product, a colourless oil, had b.p. 92°/2mm.

Nitrohemimellitenes. A mixture of 4-nitro- and 5-nitrohemimellitenes was prepared by nitration of hemimellitene with mixed acid. 40ml hydrocarbon were cooled in an ice-salt bath and a mixture of 19.7ml of nitric acid (d=1.42) and 21.0ml of sulphuric acid (d=1.8) added dropwise, with stirring, over $2\frac{1}{2}$ hours, maintaining the temperature between 0 and 10°. Stirring at room temperature was continued for a further three hours. The mixture was then poured on to crushed ice, dichloromethane added, the mixture stirred and the organic layer separated. The aqueous layer was extracted with dichloromethane, the extracts combined and washed with water, 10% aqueous sodium hydroxide and water, dried ($MgSO_4$) and distilled. The yellow distillate boiling between 102-110°/2mm was fractionated through a Nester-Faust 18" spinning band column, taking 2ml fractions.

4-Nitrohemimellitene was obtained from two recrystallisations of fractions 3-12 from 50-70° petroleum ether at -50°. The infrared spectrum was

identical with the published spectrum.[128]

5-Nitrohemimellitene was obtained by recrystallisation of the solid fractions and the still-pot residue. Treatment with decolourising charcoal in 50-70° petroleum ether and two recrystallisations from methanol gave yellow crystals, m.p. 66-67°,(lit.[128] 64-65°).

Dolinsky et al.[128] identified 5-nitrohemimellitene by its analysis and the fact that its infrared spectrum was consistent with the structure. The nuclear magnetic resonance spectra of the two nitrohemimellitenes obtained in this work are in agreement with the assignment. The 4-isomer shows an aromatic AB quartet centred at δ = 7.1 p.p.m., corresponding to the two non-equivalent 5- and 6-protons. In the 5-isomer the two aromatic protons are equivalent and a single peak at δ = 7.7 p.p.m. is obtained.

3,4,5-Trimethylphenyl acetate was prepared from recrystallised commercial 3,4,5-trimethylphenol (m.p. 108-109°, lit.[121] 107°) in 78% yield by treatment with sodium hydroxide and acetic anhydride.[125] The product had m.p. 58-58.5° after two recrystallisations from 50-70° petroleum ether. (lit.[121] 59-60°).

Nitropseudocumenes. Pseudocumene was nitrated by a method similar to that described for hemimellitene, using 69ml hydrocarbon, 35ml concentrated sulphuric acid and

33ml nitric acid (d=1.42) at 0° for 3 hours. After extraction, the crude product was distilled at 1mm; between 90-100° the distillate was an oil, and between 100-110° it solidified in the condenser. The solid product was almost pure 5-nitropseudocumene (infrared spectrum). The liquid distillate gave an infrared spectrum characteristic of a mixture of 3-nitro- and 6-nitropseudocumenes, with peaks at 1580cm^{-1} and 1260cm^{-1} characteristic of the nitro esters noted by Dolinsky.[128] The esters were removed by heating the liquid distillate with 50ml 1:1 water-ethanol for 1½ hours on a steam bath, extracting the mixture with ether, and washing the extract with 50% aqueous sodium hydroxide to remove the 3,4-dimethylbenzyl alcohol. Evaporation of the ether and distillation of the residue gave a product showing no trace of nitro ester in the infrared spectrum. Partial separation of the two nitro isomers was achieved by fractionation through an 18" Nester-Faust spinning band column.

5-Nitropseudocumene was obtained from the solid distillate by three recrystallisations from methanol as white crystals, m.p. 70-70.5° (lit.[128] 71-72°), with infrared spectrum identical to the published spectrum.[128]

3-Nitropseudocumene. The fractions from the spinning band column (b.p. 67-68°/½mm) containing the largest proportion of this isomer (infrared spectrum and gas chromato-

graph) were separated on the Megachrom to give 1.5gm of pure 3-nitropseudocumene, with infrared spectrum identical to the published spectrum.[128]

6-Nitropseudocumene was obtained by recrystallisation (from 50-70° petroleum ether) of the fractions from the spinning band column containing the largest proportion of this isomer. Two recrystallisations at -50° (dry ice-acetone) gave crystals, m.p. 20-22° (lit.[128] 19-20°) with infrared spectrum identical to the published spectrum.[128]

2,4,5-Trimethylphenyl acetate was prepared from commercial 2,4,5-trimethylphenol (m.p. 96°, lit.[121] 95-96°) by treatment with sodium hydroxide and acetic anhydride.[125] The product contained phenol (infrared spectrum) which was removed by passing the mixture in benzene down a column of 5% acetic acid-deactivated alumina to give 0.8gm phenol and 5.1gm acetate, b.p. 240-244° (lit.[121] 241°), 65% yield.

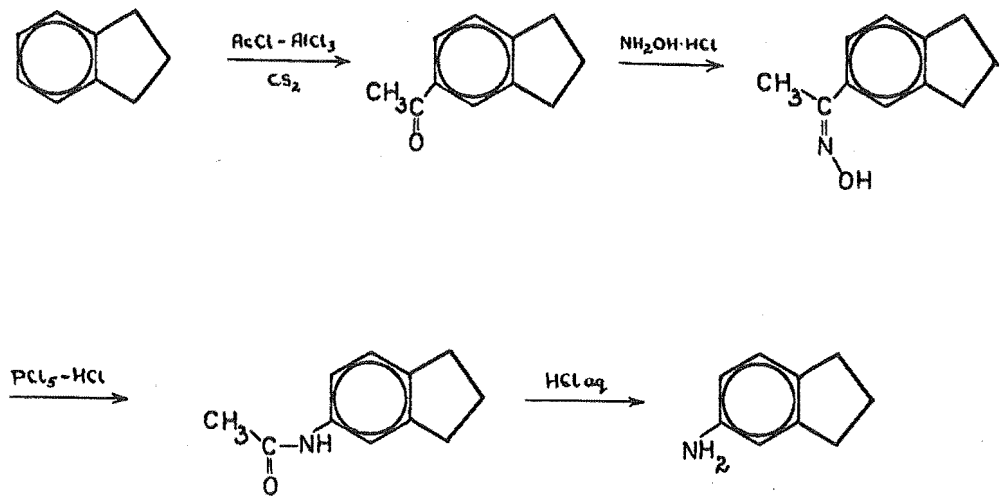
2,3,5-Trimethylphenyl acetate was prepared from recrystallised commercial 2,3,5-trimethylphenol (m.p. 72-72.5°, lit.[121] 70.5-71.5°) by treatment with sodium hydroxide and acetic anhydride.[125] It had b.p. 240-245° (lit.[121] 241°).

Nitroindans. Nitration of indan by mixed acid proved impossible to control, but the reaction was successfully carried out in acetic acid as solvent. Attempts to isolate useful quantities of 4-nitro- and 5-nitroindans from the

resulting mixture on the Megachrom were unsuccessful. The two isomers have very similar retention times, and it was necessary to inject less than 0.1gm to achieve satisfactory resolution. 4-nitroindan was obtained from the Megachrom by using a sample of the two isomers in which the 4-isomer had been concentrated by preliminary fractionation. The 5-isomer was synthesised by the method described below.

4-Nitroindan. 93ml fuming nitric acid and 51ml glacial acetic acid were stirred in an ice bath, and 25ml indan added over 1 hour, maintaining the temperature between 20 and 25° with the ice bath. The reaction was quenched in water, extracted with ether, the extract washed with water, 10% aqueous sodium carbonate and water, dried ($MgSO_4$) and distilled. The material boiling between 120-140°/2mm (20ml) was fractionated in a Nester-Faust 18" spinning band column, and the first 10ml distillate refractionated to give 4ml containing a high proportion of 4-nitroindan. From this material on the Megachrom 1.5gm 4-nitroindan was obtained, m.p. 40-40.5° after two recrystallisations from 50-70° petroleum ether. (lit.[121] 44°)

5-Nitroindan was prepared from 5-aminoindan, synthesised by a method based on the work of Baker.[129] This synthesis depends on the first step giving the 5-acetylindan with no 4-isomer, and gas chromatographic analysis confirmed this. Baker's method for the Beckmann



rearrangement gave low yields, and a method adapted from work by Roberts and Chambers[130] was used. The oxidation of the amine was carried out with peracetic acid, using a method developed by Emmons.[131]

(i) 5-Acetylindan. Indan(100gm), carbon disulphide (800ml) and acetyl chloride(80gm) were cooled in an ice bath and aluminium chloride(120gm) added with stirring over one hour. The mixture was refluxed gently until evolution of hydrogen chloride ceased, and the hot solution was poured on to a mixture of hydrochloric acid (33%, 400ml) and ice(400gm) and stirred until the aluminium salts dissolved. The carbon disulphide layer was separated, the solvent removed under vacuum, the mixture dissolved in ether, dried ($MgSO_4$) and distilled. The product boiled at 138-142°/13mm (lit.[132]

134-135°/11mm). Yield 103gm, (76%).

(ii) 5-Indanyl methyl ketoxime. 5-Acetylindan (100gm) was dissolved in ethanol (500ml) and water (300ml), and hydroxylamine hydrochloride (75gm) and sodium acetate (200gm) added. The mixture was refluxed for four hours on a steam bath, the white crystals filtered, washed with water and dried. Yield 109gm (99%), m.p. 116.5-117.5°, (lit.[132] 119°).

(iii) N-acetyl-5-aminoindan. 5-Indanyl methyl ketoxime (109gm) was dried under vacuum and suspended in dry ether on an ice bath. Phosphorus pentachloride (75gm) was added with stirring over two hours. The mixture was stirred for a further ½ hour, poured on to ice and the ether layer separated. The aqueous layer was extracted twice with ether, the total extract washed with aqueous sodium carbonate, dried and the solvent removed. The white crystals of N-acetyl-5-aminoindan after recrystallisation from ligroin, had m.p. 106° (lit.[132] 108°). Yield 65gm (60%).

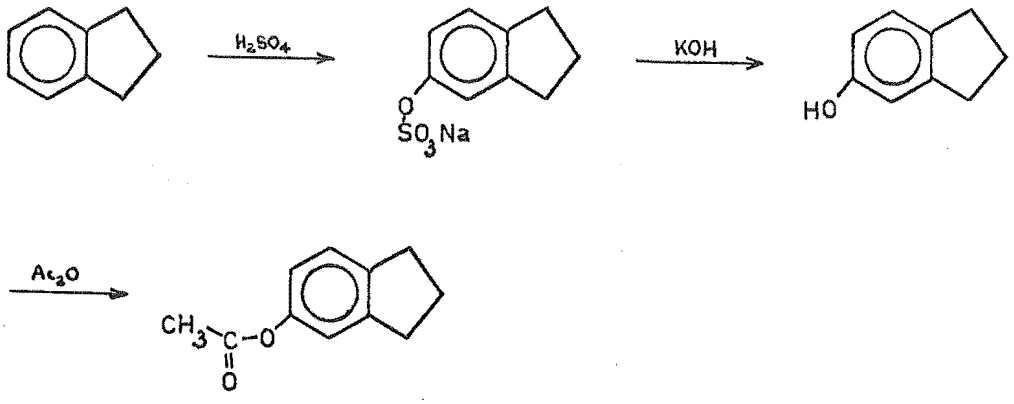
(iv) 5-Aminoindan. N-acetyl-5-aminoindan (20gm) was dissolved in ethanol (30ml) and boiled gently for four hours with hydrochloric acid (33%, 100ml). The mixture was poured on to ice, made alkaline with sodium hydroxide, extracted with ether and dried ($MgSO_4$). Distillation gave a solid which after one recrystallisation from ligroin had m.p. 36-37° (lit.[132] 37°). Yield 6.5gm (43%).

(v) 5-Nitroindan. Chloroform (30ml) was stirred vigorously on an ice bath and hydrogen peroxide (90-95%, 7ml) and sulphuric acid (1 drop) added. Acetic anhydride (30ml) was then added dropwise over $\frac{1}{2}$ hour and the flask removed from the ice bath. The opalescent solution rapidly became hot and cleared. Chloroform (20ml) was added and the mixture brought rapidly to boiling. 5-Aminoindan (6.5gm) in chloroform (13ml) was added over 15 minutes, the heat of reaction keeping the liquid boiling without external heating. The solution was refluxed for one hour, poured on to water, and the organic layer separated, washed with water, 20% aqueous sodium hydroxide, 10% hydrochloric acid, and water, dried ($MgSO_4$) and distilled to give 3.1gm (36%) of yellow solid. Recrystallisation from 50-70° petroleum ether gave white crystals, m.p. 38-39° (lit.[132] 40-40.5°).

The observed melting points of the two nitroindans are not sufficiently different to allow positive identification. The infrared substitution patterns in the 650-900cm^{-1} region of the spectrum must be treated with caution in assigning structures to aromatic nitro compounds; the nitroindans both show quite complex absorptions in this region, with major bands at 730cm^{-1}, 800cm^{-1} (4-nitro) and 810cm^{-1}, 870cm^{-1} (5-nitro), corresponding to 1,2,3-trisubstitution and 1,2,4-trisubstitution respectively. The NMR spectra allow unambiguous characterisation. Both

isomers show five peaks centred at δ =2.2 (1:4:6:4:1) corresponding to the central methylenic protons. In the 5-nitro compound the other two equivalent methylene groups appear as a triplet at δ =3.0, while in the 4-nitro compound these appear as two triplets centred at δ =3.0 and 3.4. The three aromatic protons absorb in two sets at δ =7.4 and 7.9 in both compounds, proton ratio 1:2 in the 4-isomer and 2:1 in the 5-isomer corresponding to the shift of one proton in moving from 4-nitroindan with one proton ortho to the nitro group to 5-nitroindan with two ortho protons.

5-Indanyl acetate was prepared by the following synthesis.[133]



(i) Indan-5-sulphonic acid, sodium salt. Concentrated sulphuric acid (50ml) was added slowly to indan (50ml) stirred in an ice bath. Stirring was continued at room temperature for 12 hours. The mixture was poured into water (25ml) and allowed to cool, the resulting solid mass broken up, filtered at the pump and dried under vacuum.

Attempts to recrystallise the acid in 20% sulphuric acid[133] hydrolysed much of the product. The solid was dissolved in water, neutralised with solid potassium hydroxide and the solution chilled. The white sodium sulphonate was filtered, dried at the pump and oven-dried at 110°. Yield 40gm (47%).

(ii) 5-Indanol. Indan-5-sulphonic acid, sodium salt (45gm), finely powdered and mixed with zinc dust (2.25gm), was added over ten minutes to potassium hydroxide (330gm) melted in a copper pot and maintained at 260-300°. The mixture was stirred after each addition, and for a further 20 minutes at 260°. When cool, the solid was dissolved in water (800ml) and acidified slowly with concentrated hydrochloric acid. The acid solution was extracted three times with ether, the extracts washed with water, 10% aqueous sodium carbonate and water, dried ($MgSO_4$) and the solvent removed. Distillation gave white crystals, b.p. 102-104°/1mm, m.p. 53-54° after two recrystallisations from 50-70° petroleum ether (lit.[121] 54°). Yield 6.6gm (12%). The infrared spectrum of the product was identical with the published spectrum.[134]

(iii) 5-Indanyl acetate. 5-Indanol (6.0gm) was treated with acetic anhydride and sodium hydroxide to give 5.5gm (66%) 5-indanyl acetate, b.p. 126-130°/2mm (lit.[132] 136°/18mm), showing no O-H band in the infrared.

5-Nitrotetralin was prepared from the amine by per-acetic acid oxidation as described for 5-nitroindan. 5,6,7,8-Tetrahydro-1-naphthylamine (L.Light and Co.) was freshly distilled, b.p. 125-127°/3mm (lit.[132] 146°/12mm) and oxidised to give 5.3gm (60%) 5-nitrotetralin, m.p. 31-32° after two recrystallisations from methanol (lit.[121] 34°).

6-Nitrotetralin was prepared from the amine by per-acetic acid oxidation. 5,6,7,8-Tetrahydro-2-naphthylamine (L.Light and Co.), freshly distilled, had m.p. 39-40° (lit.[132] 38.5-39.5°). 7.4gm gave 6.0gm (70%) 6-nitrotetralin, m.p. 29-30° after one recrystallisation from methanol and two from 50-70° petroleum ether (lit.[121] 31°).

6-Tetralyl acetate was prepared by a method similar to that used for 5-indanyl acetate. Sulphonation of tetralin at 60° for several hours and fusion of the resulting sulphonic acid gave a mixture of 5- and 6-tetralols (infrared spectrum[134]), and more drastic conditions were used for the sulphonation. The 5-sulphonic acid is much less soluble in cold chloroform than the 6- acid[132] and this solvent was used to remove any small quantity of 5-acid from the sulphonation product.

(i) Tetralin-6-sulphonic acid, sodium salt. Tetralin (50ml) and concentrated sulphuric acid (50ml), stirred

together for 12 hours at room temperature, and on a boiling water bath for a further 8 hours, gave a syrup which on mixing with water (25ml) formed a solid magma. This was recrystallised three times from sulphuric acid (50%, 400ml) and dried. The solid was stirred vigorously with cold chloroform (400ml) and the suspension filtered. The acid was extracted from the chloroform into water (250ml), precipitated with concentrated sulphuric acid (250ml), filtered and dried. The sodium salt was precipitated from aqueous solution of the acid with solid sodium hydroxide, filtered and dried at 110°.

(ii) 6-Tetralol was prepared by fusion of the sodium sulphonate (30gm) as described for 5-indanol. The solid product from the final distillation was recrystallised from ligroin, m.p. 59-60°, and 50-70° petroleum ether, m.p. 53-55° (lit.[132] for the dimorphic phenol 53-54° and 60-61°). Yield 8gm (39%). The phenol showed no trace of the 5-isomer in the infrared spectrum.[134]

(iii) 6-Tetralyl acetate was prepared by acetylation of the phenol with sodium hydroxide and acetic anhydride.[125] The product, b.p. 132-133°/6mm (lit.[132] 158°/14mm) contained about 5% impurity (phenol) which was removed on the Megachrom. The final product showed no impurity on the Pye Argon.

Identification of Reaction Products

Wherever possible the Megachrom was used to isolate pure samples of each component from reaction mixtures. Nitro compounds obtained in this way were identified by comparison of their infrared spectra with published spectra and with the spectra of authentic materials, and by their physical constants. Phenyl acetates were readily recognised by their carbonyl band at 1730-1790cm^{-1} and the intense 1190-1220cm^{-1} band of the C-O bond.[135] Hydrolysis of the acetate allowed characterisation of the phenol and identification of the parent acetate.

In several cases the Megachrom could not resolve the components of a reaction mixture, or could do so only with such low sample loadings that collection of components became impossible. In these cases, samples sufficient for infrared analysis were collected from the gas density chromatograph. The spectrum, together with retention times on two columns, allowed positive identification of the material. All compounds isolated, including phenols from acetate hydrolyses, were checked for purity on two 4' columns in the Pye Argon chromatograph. (10% Apiezon L on 80-100 mesh Celite and 10% PEGA on 80-120 mesh Celite). Unless otherwise stated, only one peak was obtained on both columns.

The Figures referred to in this section are placed

after the tables of results in the Results section, pp. 129-134.

Toluene

Nitration in nitric acid-acetic anhydride gave four products (Fig. 3) separated on the Megachrom. o-, m-, and p-Nitrotoluenes were identified by their infrared spectra and retention times. p-Cresyl acetate was isolated as a colourless oil whose infrared spectrum and retention time were identical with those of authentic p-cresyl acetate. Hydrolysis of the acetate with 10% aqueous sodium hydroxide gave p-cresol, m.p. 33-34° (lit.[121] 34°), infrared spectrum identical with authentic material.

Nitration in nitric acid-nitromethane and in NO_2BF_4-sulpholane gave o-, m-, and p-nitrotoluenes identified as described above.

o-Xylene

Nitration in nitric acid-acetic anhydride gave three products (Fig. 4). 3-Nitro- and 4-nitro-o-xylene were identified by infrared spectra and retention times. 3,4-Dimethylphenyl acetate was isolated (Megachrom) as a white solid, m.p. 22° after recrystallisation from methanol. (lit.[121] 22-22.5°). The infrared spectrum and retention time were identical with those of an authentic sample. (Found: C, 73.2; H, 7.9; O, 19.3. Calc. for $C_{10}H_{12}O_2$: C, 73.2; H, 7.3; O, 19.5%). The ester was hydrolysed

with 10% aqueous sodium hydroxide to 3,4-dimethylphenol, m.p. 62.5° after one recrystallisation from 50-70° petroleum ether. (lit.[121] 62.5°). (Found: C, 78.4; H, 8.0; O, 13.3. Calc. for $C_8H_{10}O$: C, 78.7; H, 8.2; O, 13.1%). The infrared spectrum of the phenol was identical with that of an authentic sample of 3,4-dimethylphenol and with the published spectrum.[134] The Pye Argon chromatograph completely separates 2,3- and 3,4-dimethylphenyl acetates on a 4', 10% Apiezon L column at 125°; reaction mixtures run under these conditions showed no trace of the 2,3- isomer.

Nitration in nitric acid-nitromethane and in NO_2BF_4-sulpholane gave 3-nitro- and 4-nitro-o-xylenes, identified by their infrared spectra and retention times.

m-Xylene

Nitration in all three systems gave 2-nitro- and 4-nitro-m-xylene as major products (Fig. 5). These were isolated (gas density chromatograph) and shown to have infrared spectra and retention times identical with authentic materials. No trace of 5-nitro-m-xylene could be found. Nitration in nitric acid-acetic anhydride gave a small quantity of a third component which had retention times on two columns identical with those of 2,4-dimethylphenyl acetate but different from those of 2,6-dimethylphenyl acetate. This compound could not be isolated.

Hemimellitene

Nitration in nitric acid-acetic anhydride gave four products, the first two of which could not be completely resolved. (Figs. 6,7). By trapping only part of these components (Megachrom), samples were obtained containing less than 5% of the interfering material, allowing positive identification. 4-Nitrohemimellitene, isolated as a yellow oil, had infrared spectrum and retention times identical with authentic material. 5-Nitrohemimellitene isolated as a solid, had m.p. 65-66° after one recrystallisation from methanol (lit.[128] 64-65°). It had infrared spectrum and retention times identical with authentic material. 2,3,4-Trimethylphenyl acetate isolated as a colourless liquid, had b.p. 239-241° (lit.[121] 239-241°). Hydrolysis in methanol-sulphuric acid gave 2,3,4-trimethylphenol, m.p. 80.5° (lit.[121] 81°) infrared spectrum identical with published spectrum; its phenylurethan derivative melted at 127° (lit.[121] 127°). 3,4,5-Trimethylphenyl acetate isolated as a solid had m.p. 59° after one recrystallisation from 30-40° petroleum ether (lit.[121] 59-60°), infrared spectrum identical with authentic material. (Found: C, 73.4; H, 8.1; O, 19.0. Calc. for $C_{11}H_{14}O_2$: C, 74.2; H, 8.1; O, 17.9%). Hydrolysis in methanol-sulphuric acid gave 3,4,5-trimethylphenol, m.p. 106.5-107.5° after recrystallisation from 30-40° petroleum ether (lit.[121]

107°), infrared spectrum identical with authentic material. (Found: C, 79.4; H, 8.8; O, 11.8. Calc. for $C_9H_{12}O$: C, 78.8; H, 8.5; O, 12.1%). The two phenylacetates were incompletely resolved, but each showed only the isomeric compound as impurity on the Pye Argon.

Nitration in nitric acid-nitromethane and NO_2BF_4-sulpholane gave 4-nitro- and 5-nitrohemimellitene identified as described above.

Pseudocumene

Nitration in nitric acid-acetic anhydride gave a mixture of products which could not be completely resolved on either the Megachrom or the gas density instrument. (Figs. 8, 9). 5-Nitropseudocumene had m.p. 70° (lit.[128] 71-72°) after two recrystallisations from methanol. The infrared spectrum and retention times were identical with authentic material. 6-Nitropseudocumene isolated as an oil, had infrared spectrum and retention times identical with authentic material. 2,3,6-Trimethylphenyl acetate was isolated as an oil from the gas density instrument. It showed phenyl acetate bands at 1790cm^{-1} and 1190-1220cm^{-1} and a band at 840cm^{-1} consistent with a 1,2,3,4-tetra-substituted benzene. The component corresponding to the fourth peak (Fig. 9) was collected from the gas density chromatograph as an oil with an infrared spectrum characteristic of a mixture of 3-nitropseudocumene and 2,4,5-tri-

methylphenyl acetate. The Pye Argon chromatograph showed two peaks from this component (4' x 4mm column, 10% ApiezonL, 175°) which had retention times identical with authentic 3-nitropseudocumene and 2,4,5-trimethylphenyl acetate. Hydrolysis of the products from these reactions with methanol-sulphuric acid removed the acetates, leaving the three nitro isomers (Fig. 10), which were collected and identified as described above.

Although 2,3,5-trimethylphenyl acetate and 2,4,5-trimethylphenyl acetate cannot be resolved on the Pye Argon using any available liquid phase, the mixed peak is considered to contain less than 5% of the 2,3,5-isomer because of the absence, in the infrared spectrum of the mixture, of the strong band at 910cm^{-1} found in the spectrum of the 2,3,5-isomer.

Nitration in nitric acid-nitromethane and in NO_2BF_4-sulpholane gave the three nitropseudocumenes, identified as described above. (Fig. 11)

Indan

Nitration in nitric acid-acetic anhydride gave three products (Fig. 12), each isolated on the Megachrom. 4-Nitroindan had m.p. 40.5-41° after one recrystallisation from 50-70° petroleum ether (lit.[121] 44-45°, authentic sample 40-41°). 5-Nitroindan had m.p. 37-37.5° after one recrystallisation from 50-70° petroleum ether (lit.[132]

40-40.5°, authentic sample 38-39°). Reduction of 5-nitroindan with tin and HCl gave 5-aminoindan, m.p. 36-38° (lit.[132] 37-38°), acetyl derivative m.p. 105-106° after recrystallisation from hot water (lit.[132] 105-106°). Both nitro isomers had infrared spectra and retention times identical with authentic materials. 5-Indanyl acetate, isolated as a colourless oil, had b.p. 125-130°/2mm (lit.[132] 136°/18mm), and infrared spectrum and retention times identical with authentic 5-indanyl acetate. Hydrolysis in methanol-sulphuric acid gave 5-indanol, m.p. 53-53.5° after recrystallisation from 50-70° petroleum ether (lit.[121] 54°), infrared spectrum and retention times identical with authentic material.

Nitration in nitric acid-nitromethane and in NO_2BF_4 - sulpholane gave 4-nitro- and 5-nitroindans, identified as described above.

Tetralin

Nitration in nitric acid-acetic anhydride gave three products (Fig. 13). 5-Nitrotetralin was isolated as a solid, m.p. 31-31.5° after one recrystallisation from methanol (lit.[121] 34°). 6-Nitrotetralin, isolated as a solid, had m.p. 30-30.5° after one recrystallisation from methanol (lit.[121] 31°). Both nitro isomers had infrared spectra and retention times identical with authentic materials. 6-Tetralyl acetate, isolated as an oil, had infrared spectrum

and retention times identical with those of authentic material. Hydrolysis in methanol-sulphuric acid gave 6-tetralol, m.p. 59-60° after one recrystallisation from 50-70° petroleum ether (lit.[132] 61-62°), infrared spectrum identical with authentic material.

Nitration in nitric acid-nitromethane and in NO_2BF_4-sulpholane gave 5-nitro- and 6-nitrotetralin. These were identified as described above.

Reaction Procedure

All reactions for analysis were carried out in the apparatus shown in Fig. 14. The tap of the dropping funnel was lubricated with Dow-Corning Silicone Stopcock grease, which resisted attack by the nitrating mixtures used. In general, five identical reactions were carried out at the same time. The flasks were clamped in a lagged bath containing ice-water for reactions at 0°, or water thermostatted to $25^{\circ} \pm 0.25^{\circ}$. Hydrocarbon, dissolved in the solvent, was stirred mechanically in the flask until the mixture reached bath temperature, then the nitrating mixture was added dropwise with continuous stirring. When the reaction time had elapsed the mixture was quenched with water (50ml), extracted twice with ether (20ml), the ether extract washed twice with water, dried over anhydrous magnesium sulphate and the drying agent removed by filtration through a sintered glass funnel. The solvent was removed at 80° under vacuum with a rotary evaporator, and the resulting samples used for analysis.

Table XIII gives the compositions of the mixtures used, and the reaction times.

Reaction Vessel

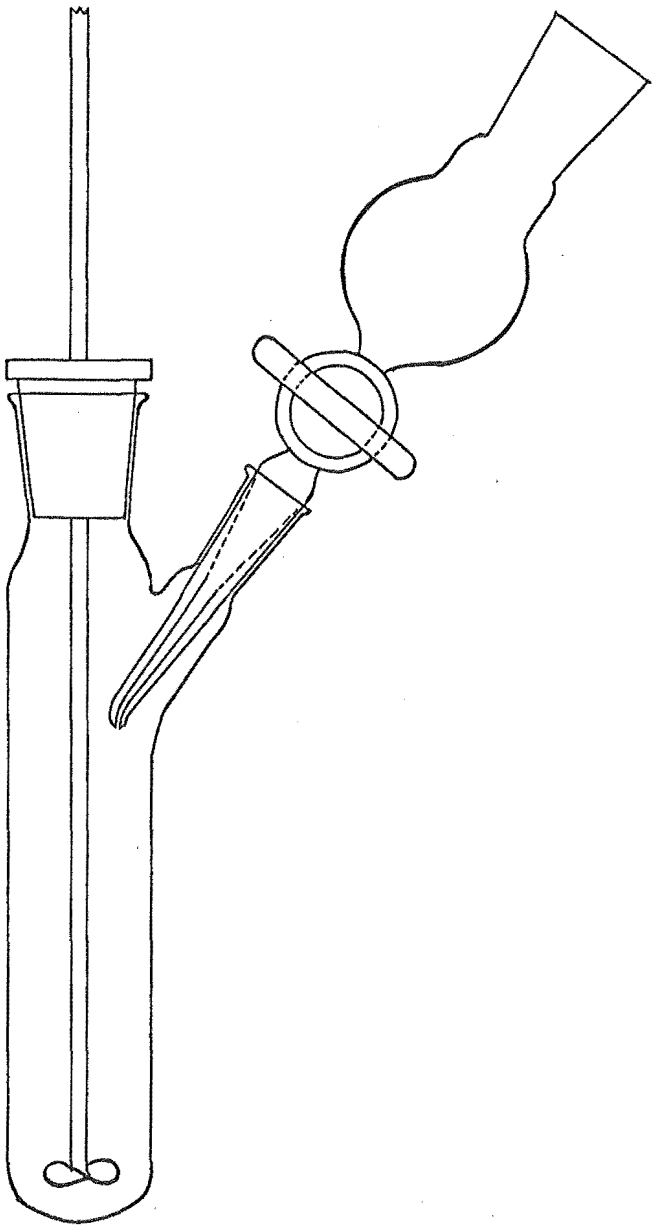


FIG. 14

TABLE XIII

Composition of reaction mixtures and reaction times.

System	Contents of Reaction Vessel	Contents of Funnel	Mixing Time	Total Reactn Time	Temp. °C
HNO_3-Ac_2O	1ml hydrocarbon 2ml Ac_2O	0.2ml HNO_3 1ml Ac_2O	½ hr.	1½ hr.	0°
HNO_3-$MeNO_2$	1ml hydrocarbon 5ml $MeNO_2$-H_2SO_4 [a]	1ml HNO_3 2ml $MeNO_2$	½ hr.	1½ hr.	0°
NO_2BF_4-sulpholane	1ml hydrocarbon 5ml sulpholane	2ml NO_2BF_4-sulpholane soln. [b]	½ hr.	½ hr.	25°

[a] The nitromethane-sulphuric acid mixture was a standard solution 0.08M in sulphuric acid.

[b] The NO_2BF_4-sulpholane solution was a standard solution 0.63M in NO_2BF_4.

Effect of changing reaction conditions

Volumes of liquids used were measured with B-grade pipettes, and for convenience the same volume of each hydrocarbon was used in all reactions. The three reaction systems did not have corresponding reagents at equivalent concentrations. It is important therefore that the reactions are insensitive to changes in reactant concentrations over

reasonable ranges. Tables XIV to XVI show this to be so.

TABLE XIV*

Product distribution from the reaction of o-xylene with nitric acid-acetic anhydride at 0°. Changes in reactant concentrations.

	[o-Xylene]+ (mole l^{-1})	[HNO_3]+ (mole l^{-1})	Product analysis A	B	C
*	2.73	1.6	56.7	14.0	29.4
	2.0	1.6	56.2	14.9	28.9
	4.1	1.6	56.8	15.0	28.3
	5.6	1.6	57.8	13.3	29.0
	2.73	0.2	55.8	14.8	29.4
	2.73	2.4	55.8	13.5	30.7

* Standard reaction.

+ Concentrations in moles per litre of acetic anhydride present in final mixture.

A = % 4-acetoxy- B = % 3-nitro- C = % 4-nitro-o-xylene.

* In this and the following tables in this section, phenyl acetates are named as acetoxy derivatives of the hydrocarbons.

TABLE XV

Product distribution from the reaction of o-xylene with nitronium tetrafluoroborate-sulpholane at 25°. Changes in reactant concentrations.

[o-Xylene]$^{+}$ (mole l^{-1})	[NO_2BF_4]$^{+}$ (mole l^{-1})	Product analysis % 3-nitro-	% 4-nitro-
* 1.04	0.15	72.3	27.7
0.55	0.16	72.5	27.7
1.85	0.17	72.2	27.8
0.91	0.09	71.2	28.8
0.65	0.24	73.0	27.0

* Standard reaction mixture.

+ Concentrations in moles per litre of sulpholane present in final mixture.

TABLE XVI

Product distribution from the reaction of o-xylene with nitric acid-nitromethane at 0°.
Changes in reactant concentrations.

[o-Xylene]$^{+}$ (mole l^{-1})	[H_2SO_4]$^{+}$ (mole l^{-1})	Product analysis % 3-nitro-	% 4-nitro-
1.04	0.18	58.8	41.2
1.04	0.09	58.1	41.9
* 1.04	0.045	57.2	42.8
1.04	0.023	56.0	44.0
0.05	0.045	56.8	43.2
2.10	0.045	57.5	42.5

* Standard reaction

+ Concentrations in moles per litre of nitromethane present in final mixture.

Effect of changes in temperature

Two of the reaction series, HNO_3-Ac_2O and HNO_3-$MeNO_2$, were carried out at 0°. The NO_2BF_4 nitrations must be carried out at 25° or the system solidifies. Examination of Table XXIV (p. 106) shows that the nitro:acetoxy product ratio for o-xylene is higher at 25° than at 0°, but that the ratio of the two nitro-o-xylenes is constant. Table XXXVIII (p. 121) shows that there is no significant difference in product distributions for nitration of o-xylene in nitric acid-nitromethane at 0° and at 25°.

Test of extraction procedure

It is important to show that the extraction procedure used does not alter the product distribution; i.e., that some products are not preferentially extracted. The acetoxy products might be expected to be susceptible to hydrolysis; for this reason no alkali was used during extraction. Mixtures of 3-nitro-, 4-nitro-, and 4-acetoxy-o-xylene were made up in the three reaction solvents and analysed before and after being subjected to the extraction procedure. The results are shown in Table XVII. No significant change occurs during extraction.

TABLE XVII

Test of Extraction Procedure

A. Nitro-o-xylenes in acetic anhydride

Run	Percentage before extraction			Percentage after extraction		
	3-nitro-	4-nitro-	4-acetoxy	3-nitro-	4-nitro-	4-acetoxy
1	26.3	32.3	41.4	26.2	31.8	42.0
2	48.2	21.5	30.4	48.3	21.7	30.0
3	47.9	22.3	29.8	46.9	22.5	30.1
4	48.0	21.2	30.9	48.5	20.9	30.6

B. Nitro-o-xylenes in nitromethane

Run	Percentage before extraction		Percentage after extraction	
	3-nitro-	4-nitro-	3-nitro-	4-nitro-
1	74.1	25.9	75.2	24.8
2	70.9	29.1	71.4	28.6
3	70.1	29.9	70.2	29.8
4	71.2	28.8	71.0	29.0

C. Nitro-o-xylenes in sulpholane

Run	Percentage before extraction		Percentage after extraction	
	3-nitro-	4-nitro-	3-nitro-	4-nitro-
1	74.1	25.9	75.0	25.0
2	70.9	29.1	71.2	28.8
3	70.1	29.9	71.6	28.4
4	71.2	28.8	71.5	28.5

Gas Chromatography

The two instruments used for quantitative analysis in this work were a Beckman "Megachrom" preparative gas chromatograph and an analytical instrument constructed for this investigation.

The Megachrom is the first commercial gas chromatograph capable of separating up to 15gm of a mixture in a single run. Although it has large sample-handling capacity, the instrument has disadvantages for both the preparative and analytical work carried out. A very limited choice of satisfactory liquid phases, very large column volumes and tedious and lengthy column packing and changing procedures reduce its versatility. The high percentage (35%) of liquid phase required necessitates the use of higher column and inlet temperatures than necessary with analytical instruments. This is important since many of the nitro compounds studied tend to decompose on the column and in the inlet. The small amount of carbon formed in the inlet from the first few injections appeared to accelerate decomposition of subsequent samples, particularly large preparative samples, and the inlet of the instrument became blocked with carbon. To overcome this a demountable stainless steel inlet was built and installed. This inlet was dismantled and cleaned frequently. A further consequence of this decomposition was that most high-boiling components trapped

from the instrument had either to be recrystallised or distilled.

Trapping efficiencies on the instrument tend to be low for two reasons. Firstly the high linear gas velocity through the traps causes sample loss particularly of high-boiling components which tend to fog on cooling. This was overcome very largely by the use of the re-entry trap described by Beckman.[136] Secondly, because the flow through the detector capillary and the main sample line beyond the stream splitter are not exactly matched, sample passes through the detector and the trap at different times. The time delay varies with the operating temperature. This can be overcome by calibration (trapping at different times over a series of runs) if sufficient material is available, but makes difficult effective separation of components with similar retention times.

The Megachrom may be successfully used as an analytical chromatograph. It is not particularly sensitive as only a small fraction of the total sample is detected. About 0.025gm of a component is required to produce a useful peak on a 1mV recorder at Attenuation 2. The four element katharometer has exceptionally high long-term stability and instrument conditions can be duplicated from day to day to give reproducible recorder responses. For this reason the instrument was used for the lengthy calibrations required for the nitrogen balance described on

p. 100. Calibration for recorder response is necessary, as the katharometer response varies with the component detected.

The Gas Density chromatograph

The Megachrom proved unable to completely resolve most of the reaction products studied. An analytical instrument using ¼" I.D. columns was constructed utilizing a Gow-Mac Model 091 Gas Density detector fitted with W-2 filaments and 9999C-1 power supply. The chromatograph was built to a standard isothermal, single column design using helical columns up to 20 ft. long. Flow control was provided in sample and reference gas lines by rotameters, and column temperature control by a Fielden TcB7 controller with a switching differential of 0.5°. The detector oven temperature was set by varying the voltage to the elements. Sample collection from this instrument was achieved in two ways. For recording infrared spectra of eluted components a 2mm x 100mm melting point tube, connected to the detector outlet and cooled with a length of cloth soaked in acetone, proved satisfactory. Injection of 5µl of component allowed sufficient material to be collected for a good spectrum. When larger samples were required repetitive injections were made and the component collected in a 4" x ¼" test tube cooled in dry ice-acetone and flushed with carrier gas before use. The eluted gas stream

was led into the tube by a length of hypodermic needle through a silicone rubber plug. Samples collected by this method were suitable for use for NMR analysis, and for microchemical analysis after distillation to remove traces of eluted liquid phase. Centrifuging the tube allowed the sample to be collected at the bottom.

The Gas Density detector

The Gow Mac Gas Density detector is the first successful commercial model of the detector invented by Martin.[137] Although slightly less sensitive than a good katharometer, its response is directly proportional to the weight concentration of the component in the carrier gas stream, and the constant of proportionality depends only on the molecular weights of the component and the carrier gas.[138] The theory of the operation of this detector has been described by Littlewood.[139] If the peak area for a component measured from the recorder trace is A, then the corrected area A^1 proportional to the weight of the component eluted is given by

$$A^1 = KA$$

where K is the area factor for the component. K is given by the expression

$$K = \frac{M_c}{M_c - Mg}$$

where M_c is the molecular weight of the component and Mg

of the carrier gas. The weight percent of any component in the mixture is given by

$$\text{Wt \% component 1} = {}^{A_1^1}/_{A_1^1 + A_2^1 + A_3^1 + \ldots.}$$

Thus if the molecular weight of each component is known, the composition of the mixture can in theory be found without calibrating the instrument. Values of K used in this work are given in Table XVIII.

TABLE XVIII

Correction factors (K) for the Gas Density Detector

Hydrocarbon	K for nitro compounds	K for acetoxy compounds
toluene	1.258	1.230
o-xylene	1.228	1.207
m-xylene	1.228	1.207
hemimellitene	1.205	1.188
pseudocumene	1.205	1.188
indan	1.208	1.190
tetralin	1.188	1.173

Calibration of the Gas Density detector

The only published study of the behaviour of the Gow-Mac detector[140] has shown that the carrier gas giving the highest sensitivity is carbon dioxide, closely followed by nitrogen. Nitrogen was used for all analyses carried out in the course of this work. Guilleman et al.[140] showed that

with carbon dioxide carrier gas, the detector response varies linearly with the volume of component injected up to a maximum sample size of about 5 µl. Tests reported in this paper with mixtures of chlorinated hydrocarbons such as trichloroethylene and pentachloroethane showed the weight response of the detector to be identical for all the compounds used to within about 5%. No information is available in the literature about the behaviour of the detector with higher boiling materials, and for this reason the instrument was calibrated for all the major components analysed in the course of this work. Table XIX shows the calculation and results for the calibration of 4-nitro- and 5-nitrohemimellitene and 5-acetoxyhemimellitene. The calibration curves for all the major reaction products are shown in Figs. 15 to 21. These graphs plot the corrected area A^1 for each major component in the product from a given hydrocarbon against the weight of component injected. For every hydrocarbon the weight responses of the individual components are identical to within 1% and the percentage compositions of the reaction products may therefore be obtained directly from the corrected areas. Percentages of uncalibrated minor components calculated in this way were assumed to be reliable. The calibration graphs show the detector response to be linear up to the largest weight of any component used, and thus no correction for peak size is required.

TABLE XIX

Calibration of recorder response for 4-nitro- and 5-nitrohemimellitenes and 5-acetoxyhemimellitene

Calibration mixture: 0.09885 g. 5-acetoxy- (A)
0.10795 g. 4-nitro- (B)
0.11375 g. 5-nitro- (C)
0.54298 g. benzene (solvent)

Run	Quantity injected		Wt. cpt. injected ($g \times 10^3$)			Corrected area		
	Vol (µl)	Wt. (g.)	A	B	C	A	B	C
1	50	0.04795	5.49	5.99	6.31	76.5	81.5	83.7
2	40	0.03890	4.45	4.86	5.12	62.5	69.8	70.7
3	30	0.02965	3.39	3.70	3.90	46.6	52.5	52.9
4	23	0.02315	2.65	2.89	3.05	37.6	41.0	42.9

Column: 15% PEGA on 60-80 mesh Chromosorb P.

T_C 225° T_D 230°

Table XX shows that the product ratio obtained from one sample is independent of the volume injected, and therefore of the peak heights.

TABLE XX

Variation of product analysis with volume injected

(One reaction product;
nitration of tetralin in acetic anhydride)

Volume injected (µl)	Product analysis %A	%B	%C
110	30.7	24.1	45.1
100	30.3	24.4	45.3
95	30.3	24.1	45.6
80	30.8	24.8	44.4
65	30.4	25.1	44.6
50	30.2	24.8	45.2
σ_1	0.02	0.14	0.16
σ_2	0.6	0.7	1.1

A = 6-acetoxy B = 5-nitro C = 6-nitro

σ_1 = Standard deviation from mean for results in this table.

σ_2 = Standard deviation from mean for complete analysis. (Table XXIX).

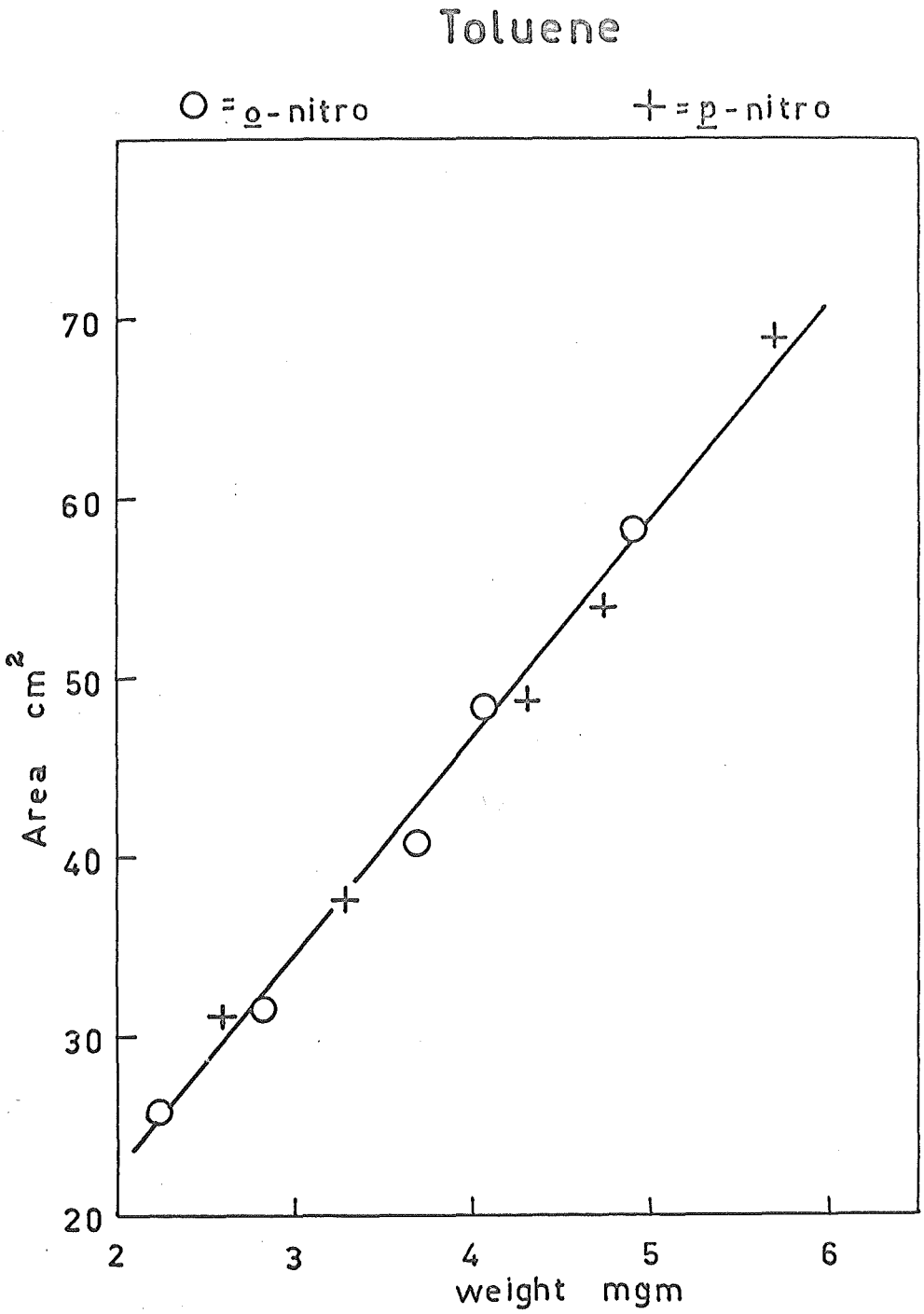

Toluene
O = o-nitro
+ = p-nitro
Area cm²
70
60
50
40
30
20
2
3
4
5
6
weight mgm

FIG. 15

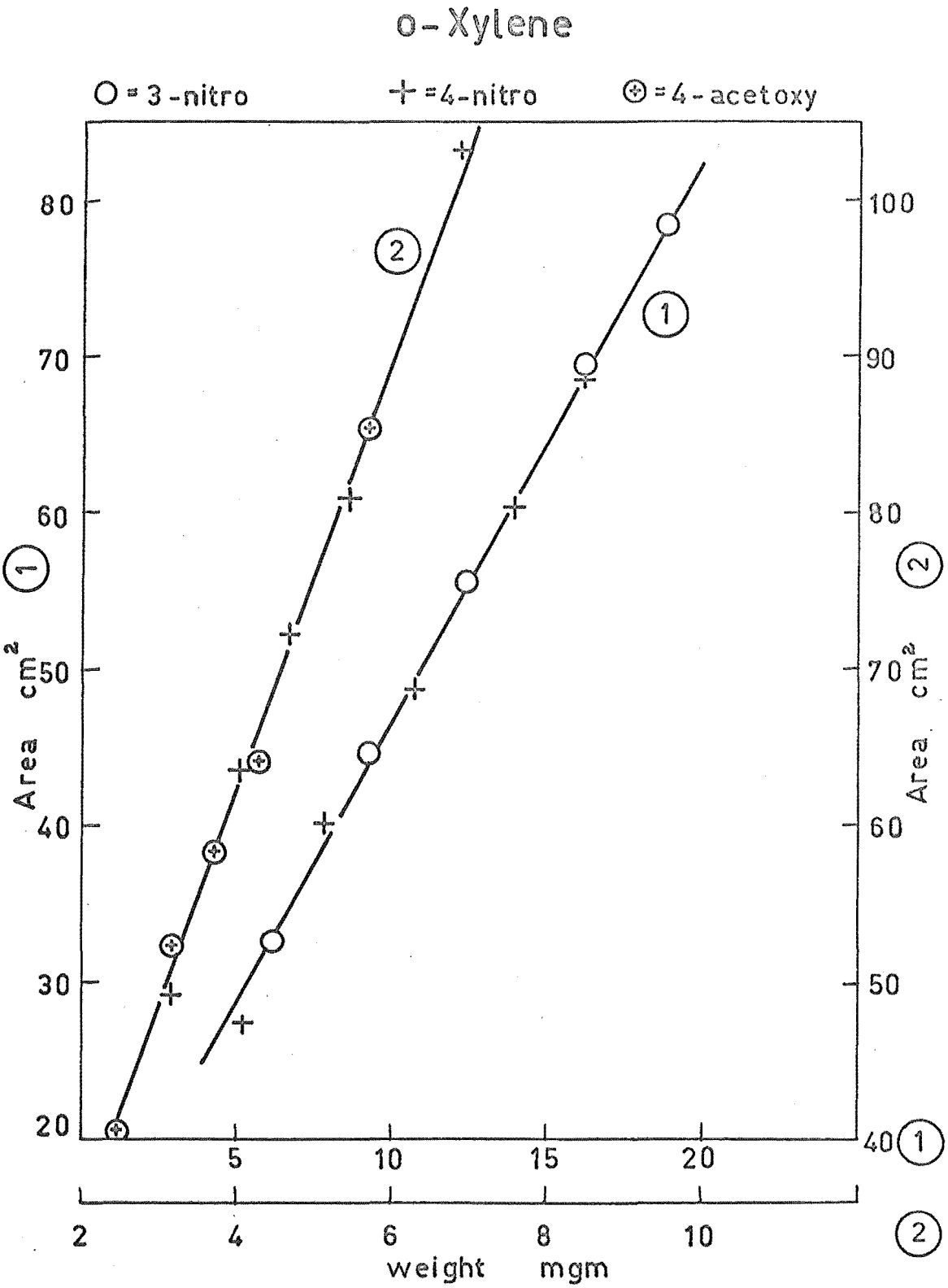

o-Xylene
O = 3-nitro
+ = 4-nitro
⊕ = 4-acetoxy
Area cm²
80
70
60
50
40
30
20
100
90
80
70
60
50
40
1
2
5
10
15
20
2
4
6
8
10
weight mgm

FIG. 16

m - Xylene

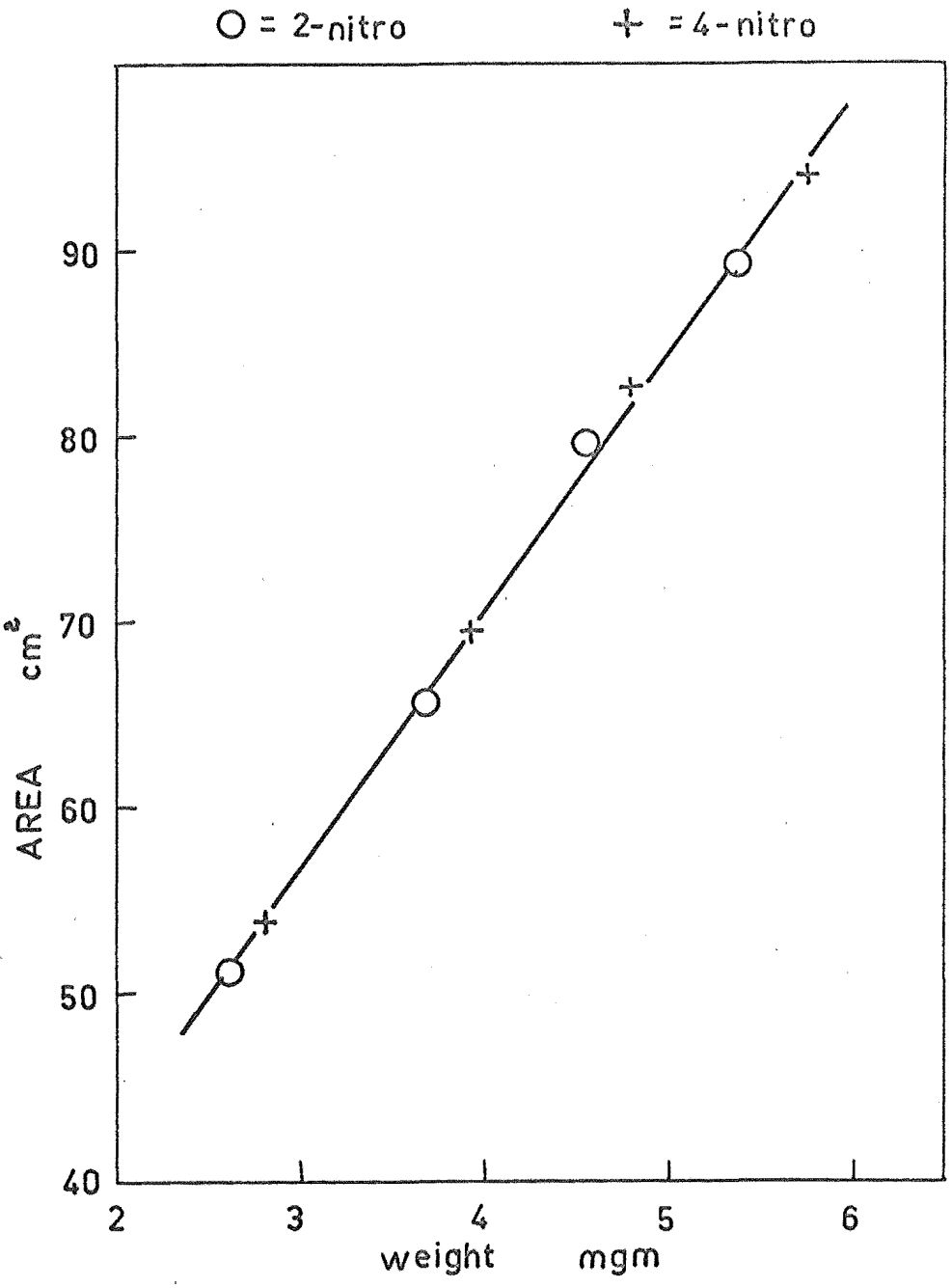


FIG. 17

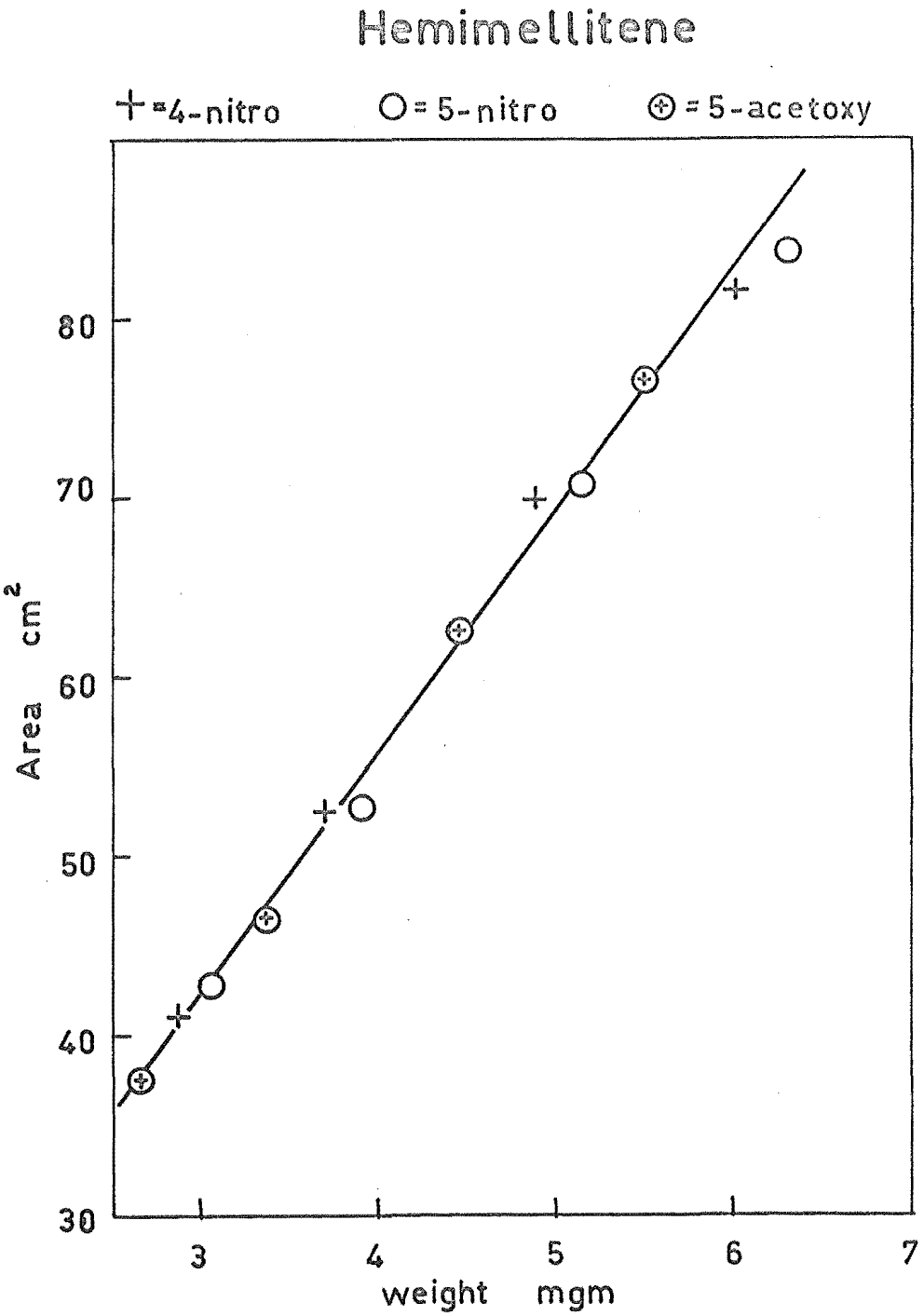

Hemimellitene
+ = 4-nitro
O = 5-nitro
⊕ = 5-acetoxy
Area cm²
80
70
60
50
40
30
3
4
5
6
7
weight mgm

FIG. 18

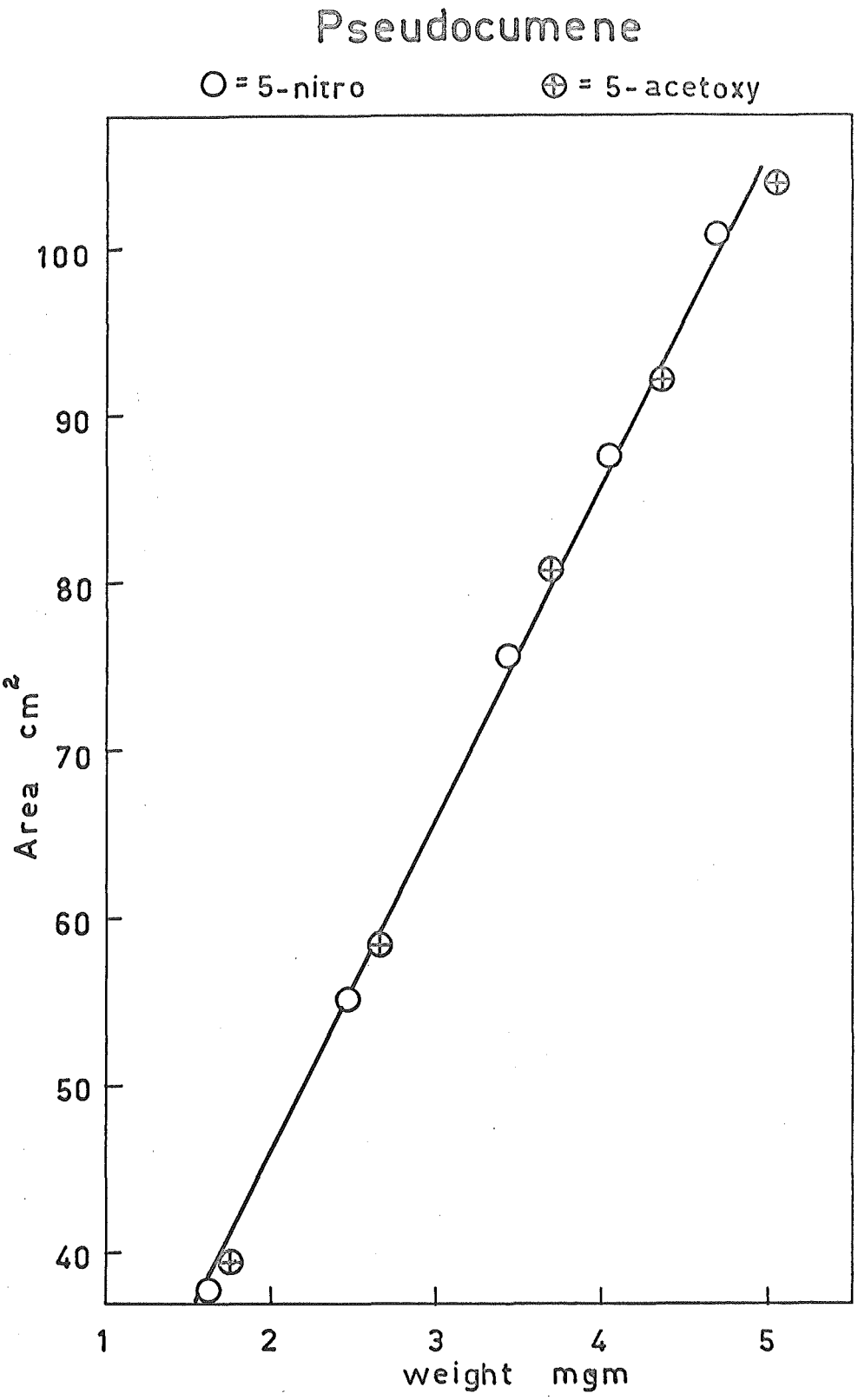

Pseudocumene
○ = 5-nitro
⊕ = 5-acetoxy
Area cm²
100
90
80
70
60
50
40
1
2
3
4
5
weight mgm

FIG. 19

Indan

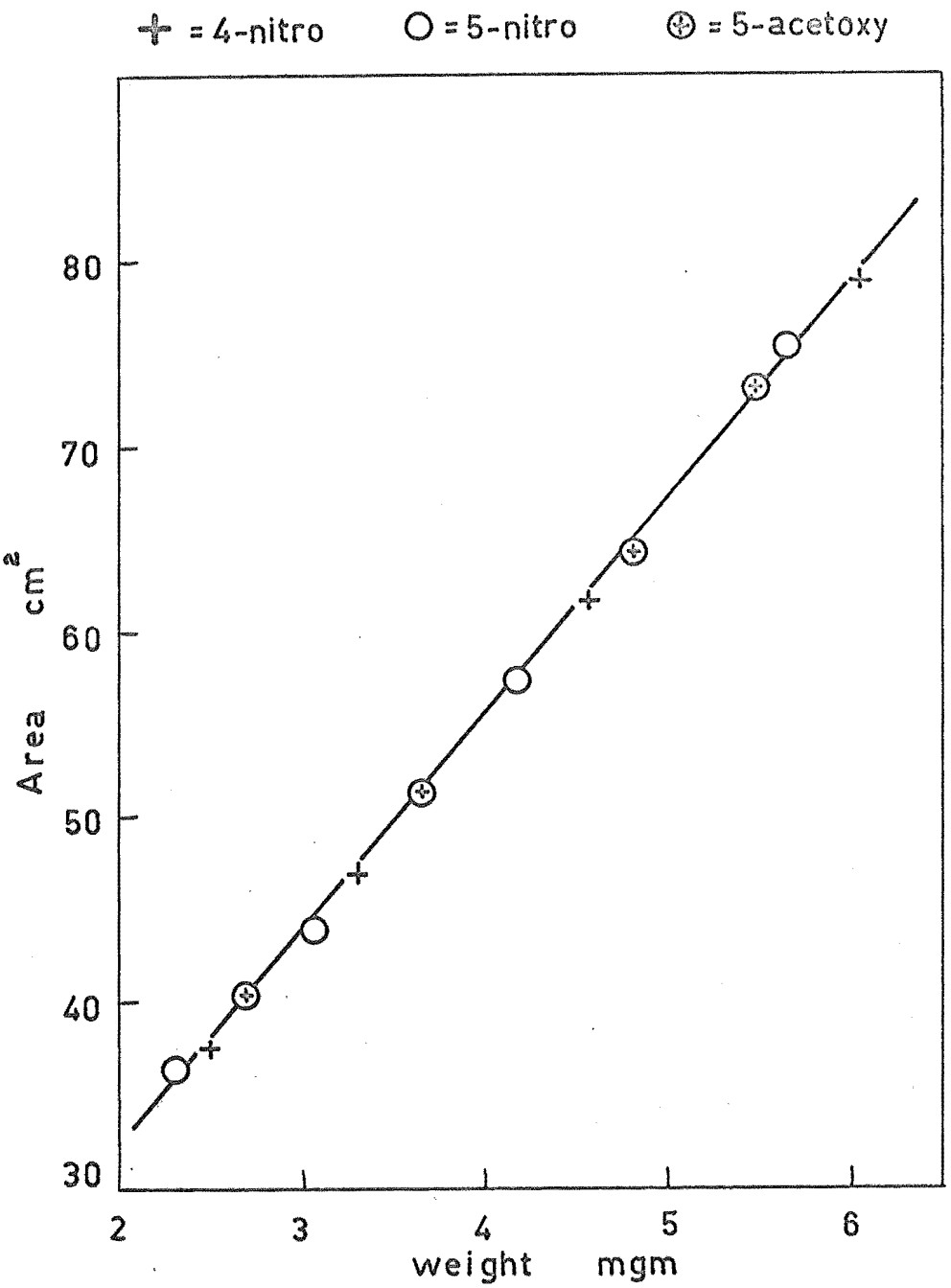

+ = 4-nitro
O = 5-nitro
⊕ = 5-acetoxy
Area cm²
80
70
60
50
40
30
2
3
4
5
6
weight mgm

FIG. 20

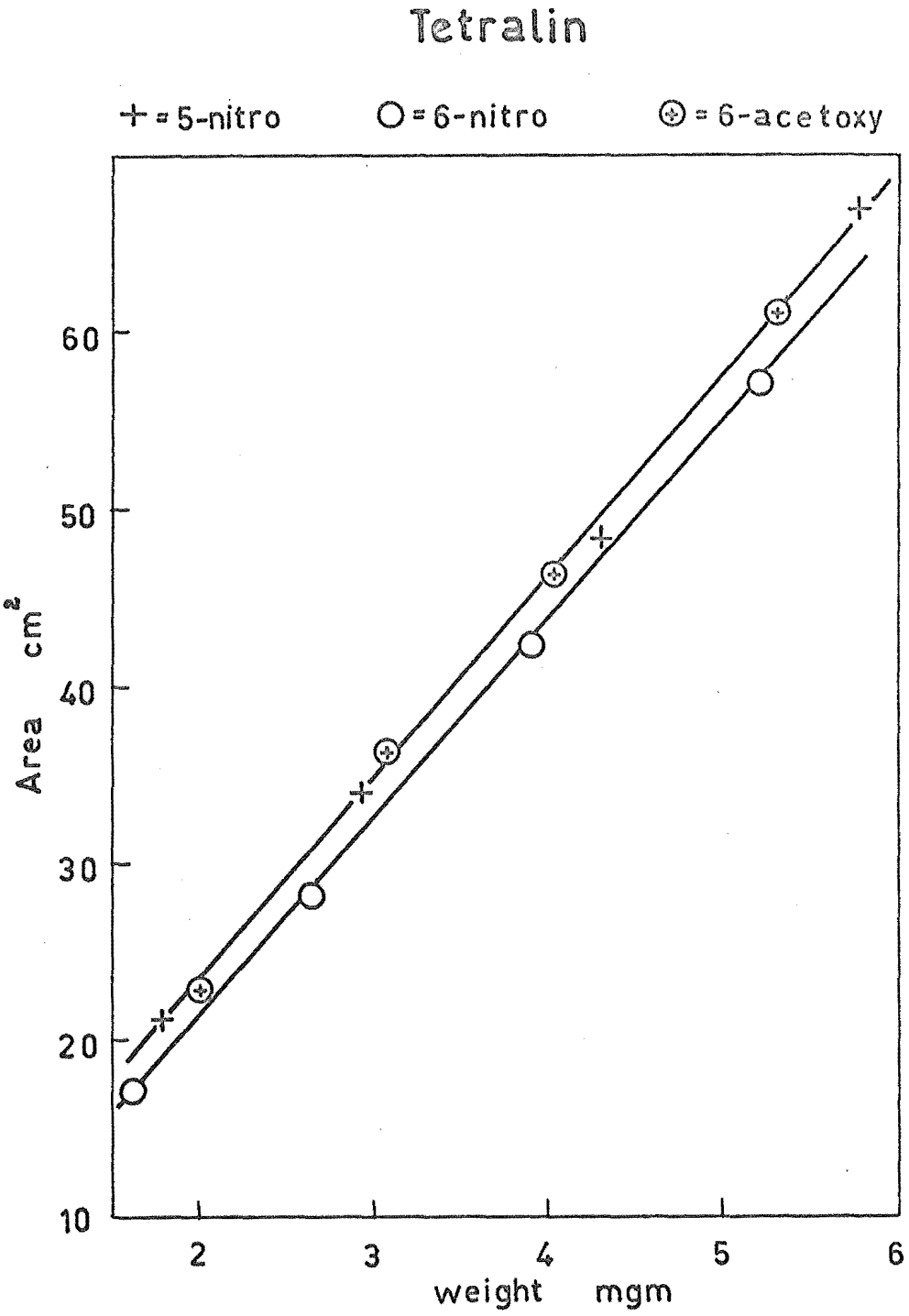

Tetralin
+ = 5-nitro
O = 6-nitro
⊛ = 6-acetoxy
Area cm²
60
50
40
30
20
10
2
3
4
5
6
weight mgm

FIG. 21

Measurement of peak areas

Peak areas were calculated from the chart as the product of peak height and width at half height. This has proved to be one of the most reliable graphical methods with symmetrical peaks; column conditions used in this work were adjusted to give symmetrical peaks for all analyses. Checks on peak areas made with a planimeter gave the same product analyses in all cases. By suitable choice of chart speed the errors in measuring peak areas could be made much smaller than the deviations between results from successive reactions. Duplicate analyses on the same reaction mixture showed that the variation between different reactions in the same set was the factor limiting the precision with which the analyses could be carried out. Table XXI shows representative data.

Column conditions for chromatography

The column packing and temperature used for each analysis are specified in the tables. The most successful column packing for mixtures of acetoxy and nitro hydrocarbons was polyethyleneglycol adipate (PEGA), and for many reaction mixtures this was the only liquid phase available which would resolve the components. At the column temperatures required PEGA bleeds rapidly from the column. At temperatures above 200°, a new column was required about once each week. At 230° bleed rate was so high that the

TABLE XXI

Duplicate analyses of the same reaction mixture

A. Nitration of indan in NO_2BF_4-sulpholane

Volume injected (µl)	Product distribution %4-nitro	%5-nitro
80	57.2	42.8
80	57.2	42.8
80	57.9	42.1
80	57.7	42.3
Standard deviation for complete analysis (Table XXXV) =	1.3	1.3

B. Nitration of tetralin in acetic anhydride

Volume injected (µl)	%6-acetoxy	%5-nitro	%6-nitro
100	30.3	24.4	45.3
100	30.3	23.9	45.8
100	30.5	24.8	44.7
Standard deviation for complete analysis (Table XXIX) =	0.6	0.7	1.1

material could be detected in the infrared spectra of collected components. Other liquid phases used were phenyldiethanolamine succinate (PDEAS), Apiezon "J", and a mixture of 33% Carbowax 20M and 66% Apiezon "J". All columns were 6 ft. long and packed with 15% liquid phase by weight on either 80-100 mesh C-22 firebrick, 60-80 mesh Chromosorb P or 60-80 mesh Chromosorb P HMDS, (Chromosorb P HMDS is a Johns-Manville product, Chromosorb P, treated with hexamethyldisilazane).

Determination of nitrite formed in nitric acid-acetic anhydride mixtures.

An attempt was made to estimate the amount of nitrite formed during the reaction of o-xylene with nitric acid in acetic anhydride. The Griess-Ilosvay test for nitrite was used to estimate the nitrite formed and an internal standard used in the reactions to allow measurement of the amounts of acetoxy- and nitro-o-xylenes produced.

Estimation of nitrite. Several modifications of the Griess-Ilosvay test used by Benford and Ingold[37] were tried. The most successful procedure is described. At the completion of the reaction the mixture (about 4ml) was made up to 5ml with acetic anhydride. 1ml of this solution was quenched with 30ml sodium hydroxide (15% W/V in distilled water). The oil was removed with carbon tetrachloride and the non-aqueous layer extracted twice with sodium hydroxide solution. The total aqueous extract was made up to 100ml in a standard flask and 2ml of this solution made up to 25ml. To 1ml of this solution in a 50ml standard flask were added 1ml of a 2% solution of sulphuric acid in distilled water, 1ml of a 1% solution of sulphanilic acid in distilled water and 10ml distilled water. After 10 minutes 1ml of a 1% solution of α-naphthol in distilled water was added to the flask and the mixture made up to 50ml with 0.91 ammonia solution (BDH AnalaR).

The solution developed a deep red colour with an absorption maximum at 520mμ. Standard nitrite solutions for calibration were made up with AnalaR sodium nitrite shown to contain 99.4±0.6% theoretical NO_2^- by titration with permanganate. Measurements were made at 520mμ on a Hilger "Uvispek" spectrophotometer. The calibration graph for nitrite is shown in Fig. 22.

Estimation of acetoxy- and nitro- hydrocarbon. The Megachrom was used for these analyses because its katharometer has much better long-term stability than the gas density detector. The standard column packing, 35% W/W Apiezon "J" on 40-60 mesh C-22 Firebrick, was used. Mixtures containing known weights of 4-acetoxy-, 3-nitro- and 4-nitro-o-xylene in o-xylene solvent were made up, and weighed aliquots injected into the Megachrom under standardised conditions using an hypodermic syringe fitted with a plunger stop. Recorder response figures for these three compounds are plotted in Fig. 23. To provide a measure of the total reaction mixture injected, o-dichlorobenzene was used as an internal standard, and the recorder calibrated for this material. (Fig. 24).

Reactions were carried out in the usual way, with the use of a weighed amount of nitric acid. At the end of the reaction a weighed amount of o-dichlorobenzene was added to the mixture and the total volume made up to 5ml with

acetic anhydride. 1ml of this solution was used to estimate nitrite. The remainder was quenched and extracted in the usual way and a weighed sample injected into the chromatograph using the same column conditions as used for the calibrations. The peak area for o-dichlorobenzene allowed calculation of the fraction of total product injected, and areas and recorder response figures for the products gave the total yield of acetoxy and nitro compounds. The following is a typical calculation; Table XXII gives the results.

(a) Mean optical density of the Griess-Ilosvay samples from the reaction mixture corresponds to 1.39×10^{-4} mmoles nitrite from the calibration graph. Dilution factor is 5x1250. Hence

Total nitrite produced is 0.88mmoles.

(b) The chromatogram gives the following peak areas from an injection of 0.0943g.

o-dichlorobenzene: $6.56 cm^2$

4-acetoxy-o-xylene: $23.81 cm^2$

3-nitro-o-xylene: $5.06 cm^2$

4-nitro-o-xylene: $10.38 cm^2$

Percent of total product injected $= \frac{6.56 \times 100}{415 \times 0.0943} =$ 16.8%

Total mmoles products formed:

4-acetoxy-o-xylene $= \frac{23.81 \times 100}{82 \times 16.8} = 1.73$

3-nitro-o-xylene $= \frac{5.06 \times 100}{61.5 \times 16.8} = 0.49$

4-nitro-o-xylene $= \frac{10.38 \times 100}{60 \times 16.8} = 1.03$ 3.25mmoles

(c) Wt. nitric acid used = 0.2850g. = 4.55mmoles

TABLE XXII

Nitrogen balance for o-xylene in nitric acid-acetic anhydride.

(All columns are mmoles except the last two.)

HNO_3 used	NO_2' formed	Products formed			%HNO_3 *	NO_2'/acetoxy
		4-acetoxy	3-nitro	4-nitro		
4.55	0.88±0.13	1.73	0.49	1.03	71	0.51±0.08
4.68	0.83±0.12	1.83	0.51	1.05	72	0.46±0.07
5.16	1.68±0.25	2.56	0.73	1.37	90	0.66±0.10

* Percent nitric acid accounted for in terms of total reaction product.

Spectrophotometer Calibration

standard nitrite

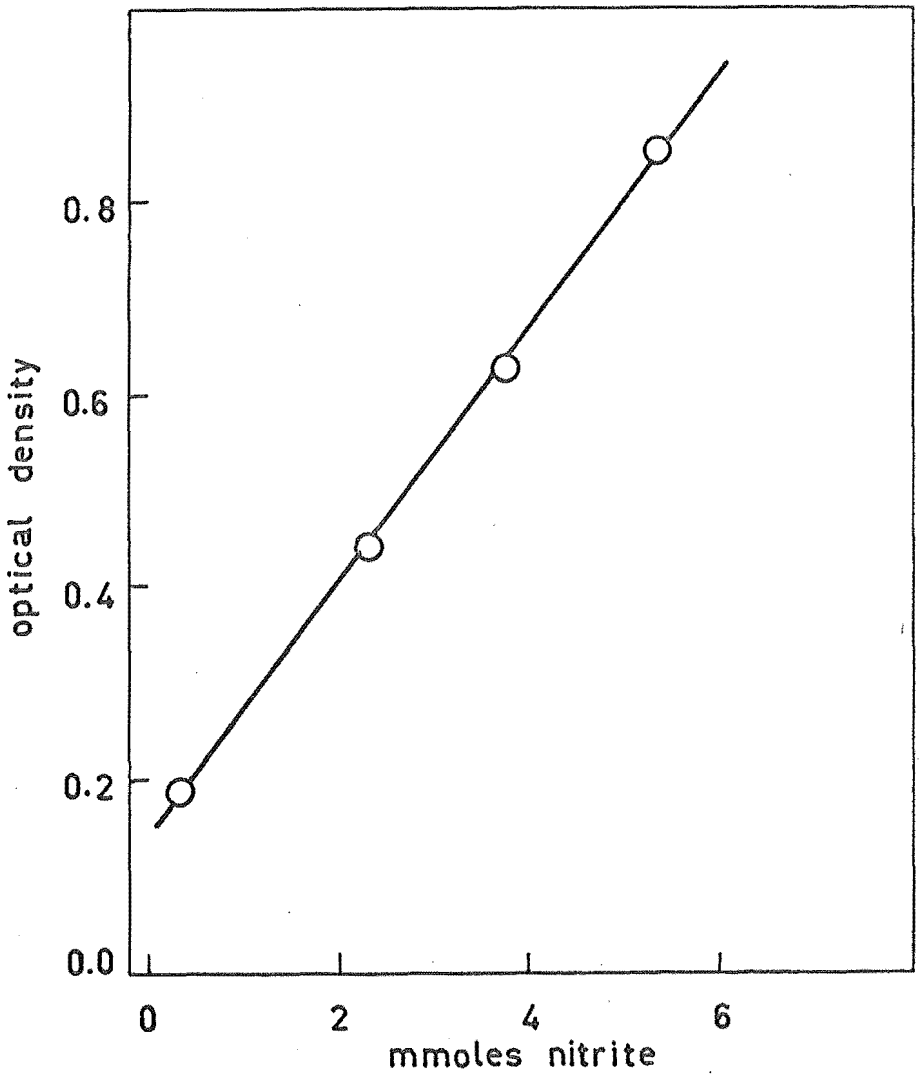


FIG. 22

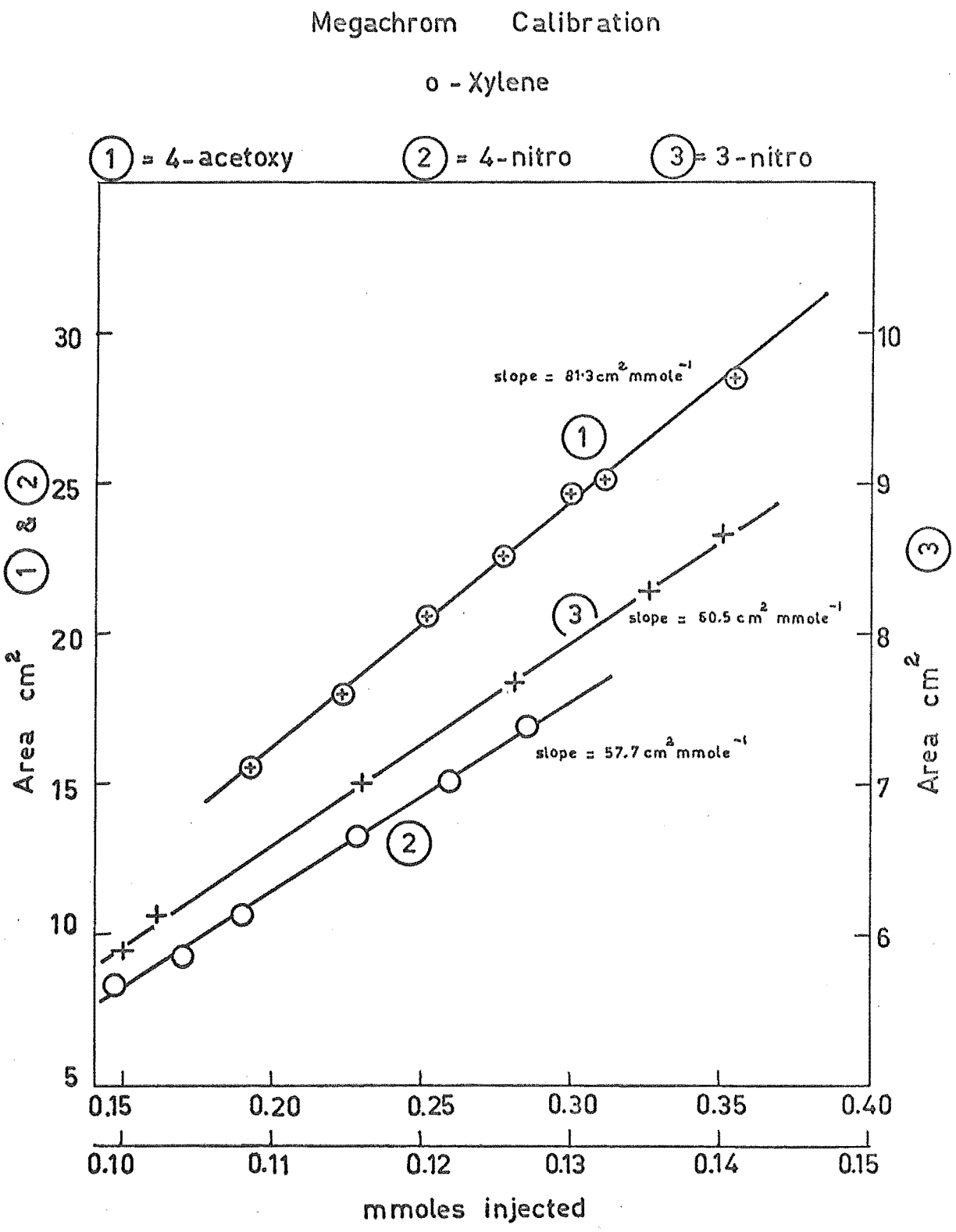

Megachrom Calibration
o - Xylene
1 = 4-acetoxy
2 = 4-nitro
3 = 3-nitro
slope = 81·3 cm² mmole⁻¹
slope = 60.5 cm² mmole⁻¹
slope = 57.7 cm² mmole⁻¹
Area cm² 1 & 2
Area cm² 3
mmoles injected
30
25
20
15
10
5
10
9
8
7
6
0.15
0.20
0.25
0.30
0.35
0.40
0.10
0.11
0.12
0.13
0.14
0.15

FIG. 23

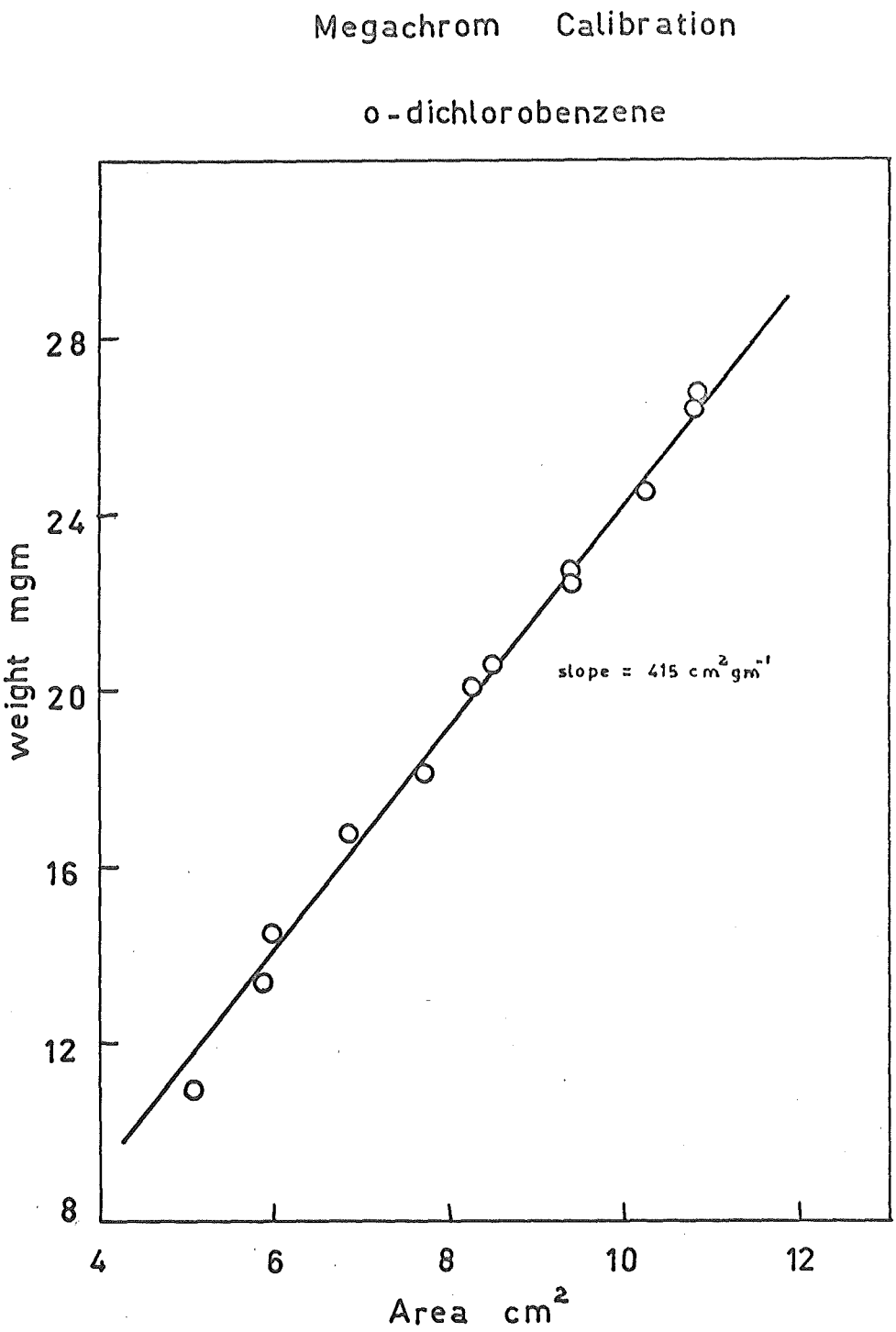

Megachrom Calibration
o-dichlorobenzene
weight mgm
28
24
20
16
12
8
4
6
8
10
12
Area cm²
slope = 415 cm² gm⁻¹

FIG. 24

RESULTS

This section contains the tabulated results and the figures showing typical chromatograms. The results, calculated by the method described in the previous section (p. 92) are weight percentages of total product. Table XXVIII also shows the chart areas and corrected areas from which the results in the table were calculated. In this section and in the Discussion, phenylacetates are named as acetoxy derivatives of the hydrocarbons to bring the numbering into line with that used for the nitro products. Thus 3,4-dimethylphenyl acetate becomes 4-acetoxy-o-xylene.

Values of σ given in the tables are the standard deviation from the mean for each set of analyses.

Chromatograph column and detector temperatures used for the analyses are given as T_C and T_D values in the tables.

TABLE XXIII

Product distribution from the reaction of toluene with nitric acid-acetic anhydride at 0°

Run	Component percentages					
	A	B	C	D	B*	D*
1	2.9	58.3	3.0	35.8	62.0	38.0
2	2.5	58.9	2.5	36.2	62.0	38.0
3	3.6	57.4	2.7	36.4	61.3	38.7
4	3.0	58.0	3.0	36.1	61.7	38.3
5	3.3	57.3	2.9	36.6	61.0	39.0
6	2.9	56.8	2.7	37.6	60.4	39.6
7	2.8	58.5	2.8	35.9	61.9	38.1
8	2.4	59.5	2.7	35.4	62.6	37.4
9	2.9	58.4	2.8	36.1	61.7	38.3
10	2.1	61.1	2.8	34.0	64.2	35.8
Mean	2.8	58.4	2.8	36.0	61.9	38.1
σ	0.35	1.2	0.45	0.9	1.06	1.06
$\pm 2\sigma$	0.7	2.4	0.9	1.8	2.1	2.1

Column: 15% PEGA on 60-80 mesh Chromosorb P

T_c 190° T_D 220°.

A = p-acetoxy B = o-nitro C = m-nitro D = p-nitro-toluene

* Calculated as percentage of B + D only.

TABLE XXIV

Product distributions from the reaction of o-xylene with nitric acid-acetic anhydride at 0° and 25°

Run	Component percentages 0°			Component percentages 25°		
	A	B	C	A	B	C
1	55.5	14.6	29.9	48.4	17.5	34.2
2	56.5	14.3	29.2	49.3	16.7	34.2
3	57.5	13.9	28.6	49.7	16.8	33.7
4	55.6	14.2	30.2	49.3	16.9	33.9
5	56.7	14.1	29.2	50.7	16.2	33.1
6	57.6	14.3	28.2	52.2	16.4	31.5
7	57.8	13.5	28.8	51.1	16.0	32.6
8	55.5	14.5	30.0	48.8	16.7	34.6
9	56.5	14.3	29.2	50.5	16.7	32.8
10	56.1	14.7	29.2	53.2	15.2	31.7
Mean	56.5	14.2	29.3	50.3	16.5	33.2
σ	0.95	0.35	0.64	1.5	0.6	1.05
$\pm 2\sigma$	1.8	0.7	1.3	3.0	1.2	2.1

Column: 15% PEGA on 60-80 mesh Chromosorb P

T_C 210° T_D 230°.

A = 4-acetoxy B = 3-nitro C = 4-nitro-o-xylene

TABLE XXV

Product distribution from the reaction of m-xylene and nitric acid-acetic anhydride at 0°

Run	Component percentages				
	A	B	C	A*	C*
1	14.6	-	85.4	14.6	85.4
2	15.2	0.7	84.1	14.6	85.4
3	14.1	0.6	85.3	14.1	85.9
4	15.0	1.1	83.9	15.0	85.0
5	13.8	0.8	85.4	14.0	86.0
6	13.9	0.6	85.5	14.0	86.0
7	13.8	0.6	85.6	13.9	86.1
8	15.9	0.9	83.2	15.8	84.2
9	15.7	0.7	83.6	15.6	84.4
10	14.7	0.8	84.5	14.7	85.3
Mean	14.7	0.7	84.7	14.6	85.4
σ	0.78	0.37	0.79	0.67	0.67
±2 σ	1.6	0.8	1.6	1.4	1.4

Column: 15% PEGA on 60-80 mesh Chromosorb P

T_C 180° T_D 230°.

A = 2-nitro B = 4-acetoxy C = 4-nitro-m-xylene

* Calculated as percentage of A + C only.

TABLE XXVI

Product distribution from the reaction of hemimellitene with nitric acid-acetic anhydride at 0°

Run	Component percentages				
	Series 1			Series 2	
	A+B	C	D	A	B
1	43.9	48.0	8.2	23.4	76.6
2	43.1	48.1	8.8	22.9	77.1
3	44.5	47.4	8.1	23.3	76.7
4	43.4	48.5	8.2	23.3	76.7
5	43.4	48.8	8.0	22.8	77.2
6	46.1	46.4	7.5	22.2	77.8
7	45.5	46.5	8.1	24.4	75.8
8	43.3	49.1	7.6	23.8	76.2
9	45.3	47.1	7.6	21.8	78.7
10	44.0	47.7	7.8	23.7	76.3
11	43.9	47.8	8.5	24.2	75.8
12	45.8	46.2	8.1	21.5	78.5
Mean	44.4	48.3	8.0	23.1	76.9
σ	1.14	1.38	0.15	0.69	1.14
$\pm 2\sigma$	2.3	2.8	0.3	1.4	2.3

Column: Series 1. 15% PDEAS on 80-120 mesh Celite. $T_C 212^\circ$ $T_D 230^\circ$.

Series 2. 15% PEGA on 60-80 mesh Chromosorb P. $T_C 187^\circ$ $T_D 230^\circ$.

A=4-acetoxy B=5-acetoxy C=4-nitro D=5-nitrohemimellitene

TABLE XXVII

Product distribution from the reaction of pseudocumene with nitric acid-acetic anhydride at 0°

Run	Component percentages			
	A + B	C	D	E
1	34.6	10.9	3.2	51.4
2	35.2	9.6	3.4	52.0
3	33.3	8.5	3.5	54.8
4	33.7	10.4	3.4	52.5
5	36,7	10.7	3.7	49.0
6	35.1	9.6	1.5	53.6
7	35.9	10.8	2.1	51.4
8	34.8	8.1	3.6	53.5
9	36.8	9.9	2.2	51.1
10	35.5	11.8	2.6	50.0
Mean	35.2	10.0	2.9	51.9
σ	1.15	1.1	0.76	1.6
$\pm 2\sigma$	2.3	2.2	1.5	3.2

Column: 15% PEGA on 80-100 mesh C-22 Firebrick.

T_C 190° T_D 225°

A = 3-nitro- B = 5-acetoxy- C = 3-acetoxy-

D = 6-nitro- E = 5-nitropseudocumene

TABLE XXVII (contd.)

Product distribution from the reaction of pseudocumene with nitric acid-acetic anhydride at 0° after acid hydrolysis

Run	Component percentages		
	A	D	E
5	13.8	7.0	79.2
6	15.8	6.3	77.9
7	15.6	7.1	77.4
8	16.9	7.5	75.6
9	15.7	7.5	76.7
10	16.1	7.1	76.7
Mean	15.7	7.1	77.3
σ	1.04	0.4	1.2
$\pm 2\ \sigma$	2.1	0.8	2.4

Column: as for first part of table.

A = 3-nitro- D = 6-nitro-

E = 5-nitropseudocumene

TABLE XXVIII

Product distribution from the reaction of indan with nitric acid-acetic anhydride at 0°

Run	Chart areas			Corrected areas			Component %ages		
	A	B	C	A	B	C	A	B	C
1	31.8	21.1	61.2	37.8	25.5	74.0	27.5	18.5	54.0
2	33.6	21.7	62.3	40.0	26.2	75.3	28.3	18.5	53.2
3	19.4	13.2	35.5	23.1	15.9	43.0	28.2	19.4	52.5
4	64.2	38.3	109.8	76.4	46.4	132.8	29.9	18.2	52.0
5	68.9	45.5	123.8	82.0	55.0	149.8	28.6	19.2	52.3
6	52.8	35.4	93.9	62.8	42.8	113.7	28.6	19.5	51.9
7	87.5	54.0	158.0	104.0	65.2	191.0	28.9	18.1	53.0
8	70.4	43.0	123.4	83.6	52.0	149.0	29.4	18.3	52.4
9	56.6	33.9	97.5	67.4	41.0	118.0	29.8	18.1	52.1
Mean							28.8	18.6	52.6
σ							0.79	0.57	0.69
$\pm 2\sigma$							1.6	1.2	1.4

Column: 5% Carbowax 20M: 10% Apiezon "J" on 60-80 mesh Chromosorb P. $T_C 255°$ $T_D 240°$.

A = 5-acetoxy- B = 4-nitro- C = 5-nitroindan.

TABLE XXIX

Product distribution from the reaction of tetralin and nitric acid-acetic anhydride at 0°

Run	Component percentages		
	6-acetoxy	5-nitro	6-nitro
1	29.6	22.7	47.8
2	30.9	24.7	44.4
3	29.4	25.0	45.8
4	30.5	24.5	45.2
5	31.0	25.4	43.6
6	30.5	24.0	45.5
7	29.9	24.1	46.0
8	31.2	24.5	44.4
9	31.2	24.2	44.5
10	30.4	24.7	44.9
11	30.2	24.5	45.4
12	30.7	24.1	45.1
Mean	30.5	24.4	45.2
σ	0.6	0.66	1.06
$\pm 2\ \sigma$	1.2	1.3	2.1

Column: 15% PEGA on 80-100 mesh C22 Firebrick

T_C 245° T_D 240°

TABLE XXX

Product distribution from the reaction of toluene with nitronium tetrafluoroborate-sulpholane at 25°

Run	Component percentages				
	A	B	C	A*	B*
1	62.4	3.2	34.4	64.5	35.5
2	63.0	3.9	33.1	65.6	34.4
3	61.4	4.3	34.4	64.1	35.9
4	63.9	3.0	33.2	65.8	34.2
5	62.1	3.4	34.5	64.4	35.6
6	63.7	3.4	32.9	66.0	34.0
7	62.0	3.5	34.5	64.2	35.8
8	64.8	2.3	33.0	66.3	33.7
9	64.9	2.4	32.8	66.5	33.5
10	60.9	3.2	35.9	63.0	37.0
Mean	62.9	3.3	33.9	65.0	35.0
σ	1.5	0.63	1.0	1.0	1.0
±2 σ	3.0	1.3	2.0	2.0	2.0

Column: 15% PEGA on 60-80 mesh Chromosorb P.

T_C 190° T_D 220°

A = o-nitro- B = m-nitro- C = p-nitrotoluene

* Calculated as percentage of A + B only.

TABLE XXXI

Product distribution from the reaction of o-xylene with nitronium tetrafluoroborate-sulpholane at 25°

Run	Component percentages	
	3-nitro-	4-nitro-
1	74.6	25.4
2	74.5	25.5
3	73.4	26.6
4	73.7	26.3
5	73.0	27.0
6	74.4	25.6
7	73.8	26.2
8	73.5	26.5
9	73.0	27.0
10	73.2	26.8
Mean	73.7	26.3
σ	0.59	0.58
$\pm 2\ \sigma$	1.2	1.2

Column: 15% PEGA on 60-80 mesh Chromosorb P

$T_C 210^\circ$ $T_D 230^\circ$.

TABLE XXXII

Product distribution from the reaction of m-xylene with nitronium tetrafluoroborate-sulpholane at 25°

Run	Component percentages	
	2-nitro-	4-nitro-
1	14.2	85.8
2	14.4	85.6
3	15.0	85.0
4	15.3	84.7
5	15.0	85.0
6	13.5	86.5
7	15.0	85.0
8	15.0	85.0
Mean	14.7	85.3
σ	0.6	0.6
$\pm 2\sigma$	1.2	1.2

Column: 5% Carbowax 20M: 10% Apiezon "J" on 60-80 mesh Chromosorb P.

$T_C 210°$ $T_D 235°$

TABLE XXXIII

Product distribution from the reaction of hemimellitene with nitronium tetrafluoroborate-sulpholane at 25°

Run	Component percentages	
	4-nitro-	5-nitro-
1	92.7	7.3
2	92.0	8.0
3	93.3	6.7
4	92.7	7.3
5	92.2	7.8
6	93.3	6.7
7	92.8	7.2
8	92.6	7.4
9	92.8	7.2
10	91.4	8.6
Mean	92.6	7.2
σ	0.6	0.6
$\pm 2\sigma$	1.2	1.2

Column: 15% PEGA on 60-80 mesh Chromosorb P

$T_C 225°$ $T_D 230°$.

TABLE XXXIV

Product distribution from the reaction of pseudocumene with nitronium tetrafluoroborate-sulpholane at 25°

Run	Component percentages		
	3-nitro-	6-nitro-	5-nitro-
1	11.0	33.3	55.7
2	9.3	34.6	56.1
3	9.2	36.0	54.9
4	8.9	34.9	56.4
5	8.5	35.1	56.6
6	8.8	35.4	55.8
7	9.6	34.4	56.0
8	8.9	34.6	56.5
9	10.0	33.3	56.7
10	9.9	35.2	55.0
Mean	9.4	34.7	56.0
σ	0.74	0.86	0.63
$\pm 2\ \sigma$	1.6	1.7	1.3

Column: 15% PEGA on 60-80 mesh Chromosorb P

$T_C 200°$ $T_D 225°$

TABLE XXXV

Product distribution from the reaction of indan with nitronium tetrafluoroborate-sulpholane at 25°

Run	Component percentages	
	4-nitro-	5-nitro-
1	55.4	44.6
2	59.3	40.7
3	57.0	43.0
4	58.4	41.6
5	59.2	40.8
6	59.3	40.7
7	59.1	40.9
8	58.8	41.2
9	59.0	41.0
10	57.2	42.8
Mean	58.3	41.7
σ	1.3	1.3
$\pm 2\sigma$	2.6	2.6

Column: 5% Carbowax 20M: 10% Apiezon "J" on 80-100 C-22 Firebrick

T_C 228° T_D 240°

TABLE XXXVI

Product distribution from the reaction of tetralin with nitronium tetrafluoroborate-sulpholane at 25°

Run	Component percentages	
	5-nitro-	6-nitro-
1	62.8	37.2
2	61.7	38.3
3	61.6	38.4
4	60.0	40.0
5	61.3	38.7
6	61.8	38.2
7	62.8	37.2
8	64.0	36.0
9	58.4	41.6
10	59.5	40.5
Mean	61.4	38.6
σ	1.7	1.7
$\pm 2\ \sigma$	3.4	3.4

Column: 5% Carbowax 20M: 10% Apiezon "J" on 80-100 mesh C-22 Firebrick

T_C 235° T_D 240°

TABLE XXXVII

Product distribution from the reaction of toluene with nitric acid-nitromethane at 0°

Run	Component percentages				
	A	B	C	A*	C*
1	62.5	2.5	35.0	64.1	35.9
2	61.1	3.4	35.5	63.2	36.8
3	61.6	2.9	35.5	63.4	36.6
4	60.6	3.0	36.4	62.5	37.5
5	61.5	3.2	35.4	63.5	36.5
6	61.5	3.3	35.3	63.6	36.4
7	61.2	3.2	35.6	63.2	36.8
8	61.4	3.2	35.5	63.4	36.6
9	61.2	3.1	35.7	63.2	36.8
Mean	61.4	3.1	35.5	63.3	36.7
σ	0.51	0.26	0.39	0.42	0.42
$\pm 2\sigma$	1.0	0.5	0.8	0.8	0.8

Column: 15% PEGA on 60-80 mesh Chromosorb P

T_C 190° T_D 220°

A = o-nitro- B = m-nitro- C = p-nitrotoluene

* Calculated as percentage of A + C only.

TABLE XXXVIII

Product distributions from the reaction of o-xylene with nitric acid-nitromethane at 0° and 25°

Run	Component percentages 0°		Component percentages 25°	
	3-nitro-	4-nitro-	3-nitro-	4-nitro-
1	57.5	42.5	58.8	41.2
2	57.6	42.4	57.6	42.4
3	56.9	43.1	56.5	43.5
4	57.3	42.7	59.7	40.3
5	57.8	42.2	59.5	40.5
6	58.6	41.4	59.8	40.2
7	59.5	40.5	60.0	40.0
8	59.8	40.2	59.7	40.3
9	59.6	40.4	60.0	40.0
10	58.9	41.1	59.8	40.2
Mean	58.4	41.6	59.1	40.9
σ	1.0	1.0	1.2	1.2
$\pm 2\ \sigma$	2.0	2.0	2.4	2.4

Column: 15% PEGA on 60-80 Chromosorb P/HMDS

$T_C 190^\circ$ $T_D 230^\circ$.

TABLE XXXIX

Product distribution from the reaction of m-xylene with nitric acid-nitromethane at 0°

Run	Component percentages	
	2-nitro-	4-nitro-
1	12.8	87.2
2	13.6	86.4
3	12.7	87.3
4	12.7	87.3
5	13.6	86.4
6	13.1	86.9
7	13.2	86.8
8	13.3	86.7
Mean	13.1	86.9
σ	0.37	0.4
$\pm 2\sigma$	0.8	0.8

Column: 5% Carbowax 20M: 10% Apiezon "J" on 60-80 Chromosorb P

$T_C 210^\circ$ $T_D 230^\circ$

TABLE XL

Product distribution from the reaction of hemimellitene with nitric acid-nitromethane at 0°

Run	Component percentages	
	4-nitro-	5-nitro-
1	84.7	15.3
2	84.5	15.5
3	84.5	15.5
4	84.5	15.5
5	85.2	14.8
6	84.5	15.5
7	84.3	15.7
8	83.8	16.2
9	83.8	16.2
10	84.8	15.2
Mean	84.5	15.5
σ	0.42	0.42
$\pm 2\sigma$	0.8	0.8

Column: 15% PEGA on 60-80 mesh Chromosorb P

$T_C 225^\circ$ $T_D 230^\circ$

TABLE XLI

Product distribution from the reaction of pseudocumene with nitric acid-nitromethane at 0°

Run	Component percentages				
	A	B	C	B*	C*
1	5.4	25.0	69.6	26.5	73.5
2	4.9	26.6	68.5	28.0	72.0
3	4.4	24.0	71.8	25.1	74.9
4	4.5	25.5	70.1	26.7	73.3
5	4.3	25.0	70.7	26.1	73.9
6	5.5	24.6	70.0	26.0	74.0
7	4.5	26.5	69.2	27.6	72.4
8	5.2	26.8	68.2	28.1	71.9
9	4.8	25.4	69.9	26.6	73.4
10	4.2	27.5	68.5	28.7	71.3
Mean	4.8	25.7	69.7	26.9	73.1
σ	0.47	1.11	1.11	1.11	1.11
±2 σ	0.9	2.2	2.2	2.2	2.2

Column: 15% PEGA on 60-80 mesh Chromosorb P

$T_C 200^\circ$ $T_D 225^\circ$

A = 3-nitro- B = 6-nitro- C = 5-nitropseudocumene

* Calculated as percentage of B + C only.

TABLE XLII

Product distribution from the reaction of indan with nitric acid-nitromethane at 0°

Run	Component percentages	
	4-nitro-	5-nitro-
1	42.0	58.0
2	41.2	58.8
3	41.8	58.2
4	41.6	58.4
5	42.5	57.5
6	41.9	58.1
7	41.3	58.7
8	42.0	58.0
9	42.7	57.3
Mean	41.9	58.1
σ	0.47	0.47
$\pm 2\ \sigma$	1.0	1.0

Column: 15% PEGA on 60-80 mesh Chromosorb P

T_C 225° T_D 240°

TABLE XLIII

Product distribution from the reaction of tetralin with nitric acid-nitromethane at 0°

Run	Component percentages	
	5-nitro-	6-nitro-
1	41.9	58.1
2	41.3	58.7
3	41.0	59.0
4	41.7	58.3
5	41.5	58.5
6	40.6	59.4
7	41.1	58.9
8	41.0	59.0
9	42.0	58.0
10	40.7	59.3
Mean	41.3	58.7
σ	0.49	0.49
$\pm 2\sigma$	1.0	1.0

Column: 15% PEGA on 60-80 mesh Chromosorb P

T_C 245° T_D 240°

Precision of results

The standard deviation from the mean σ for each component in each set of results is tabulated, together with the value of 2σ, which has been used in the discussion as the absolute error in any value. Thus in Table XXIII, p. 105, the value of 2σ for component B, o-nitrotoluene, is 2.4 and the percentage of this component is thus $58.4 \pm 2.4\%$.

Table XXVI. Nitric acid-acetic anhydride nitration of hemimellitene. The chromatograms corresponding to this table are shown in Figs. 6 and 7. The 4-acetoxy and 5-acetoxyhemimellitenes are treated as a single component in the first set of analyses (Fig. 6). The same reaction products were re-analysed (Fig. 7, Series 2) at a lower column temperature to give partial resolution of these two components. Johns[141] has examined a case very similar to this, and shown that the percentage composition calculated from the peak areas (measured by the triangulation method used here) is within 0.5% of the known composition. For this reason, and because of the good agreement between the twelve analyses in Series 2, the results are considered accurate. Combination of the two sets of results gives the final figures for this analysis (weight percent) as:

4-acetoxy	$10.2 \pm 1.1\%$	5-acetoxy	$34.0 \pm 3\%$
4-nitro	$48.3 \pm 2.8\%$	5-nitro	$8.0 \pm 0.3\%$

Table XXVII. Nitric acid-acetic anhydride nitration of pseudocumene. The chromatograms corresponding to this table are shown in Fig. 9 (before hydrolysis) and Fig. 10 (after hydrolysis). By taking the 5-nitro peak (component E) in each case as standard, combination of the two sets of results gives the final percentages:

A = 10.6; B = 24.6; C = 10.0; D = 2.9; E = 51.9%

Calculating back from these figures the nitro percentages are A = 16.2±2.5; D = 4.4±2.2; E = 79.4±2.5%

compared with the values in the second set of results

A = 15.7±2; D = 7.1±0.8; E = 77.3±2.4%.

The two sets of values are therefore consistent; the small area corresponding to component D is more difficult to measure in the first set of results and the figures from the second set are therefore used when only the nitro ratios are required.

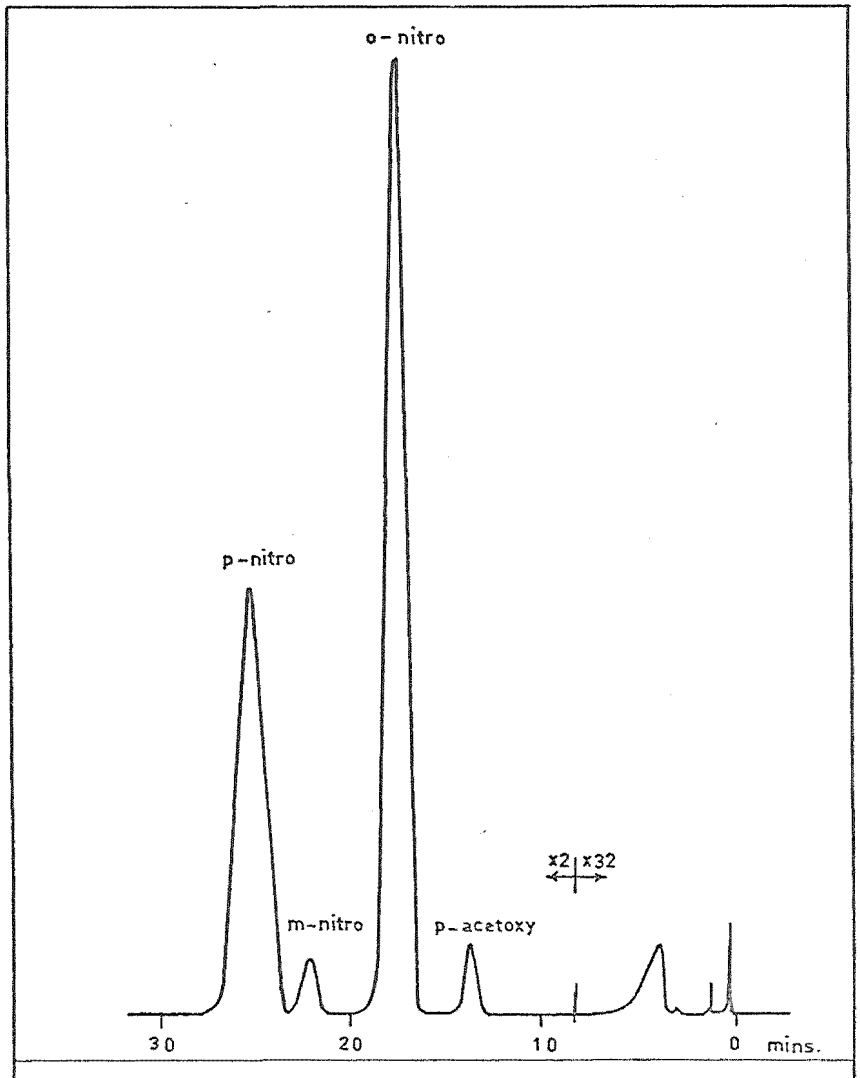


FIG. 3 Toluene - Ac_2O

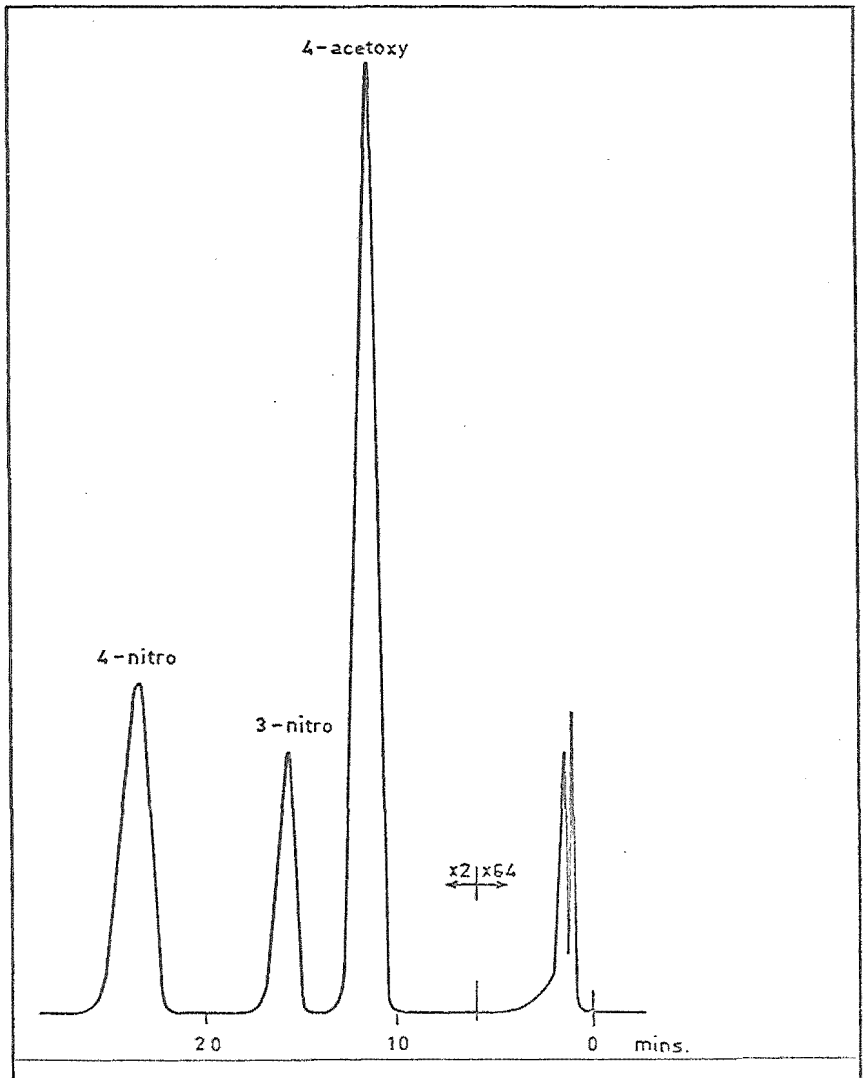


FIG. 4 o-Xylene - Ac_2O

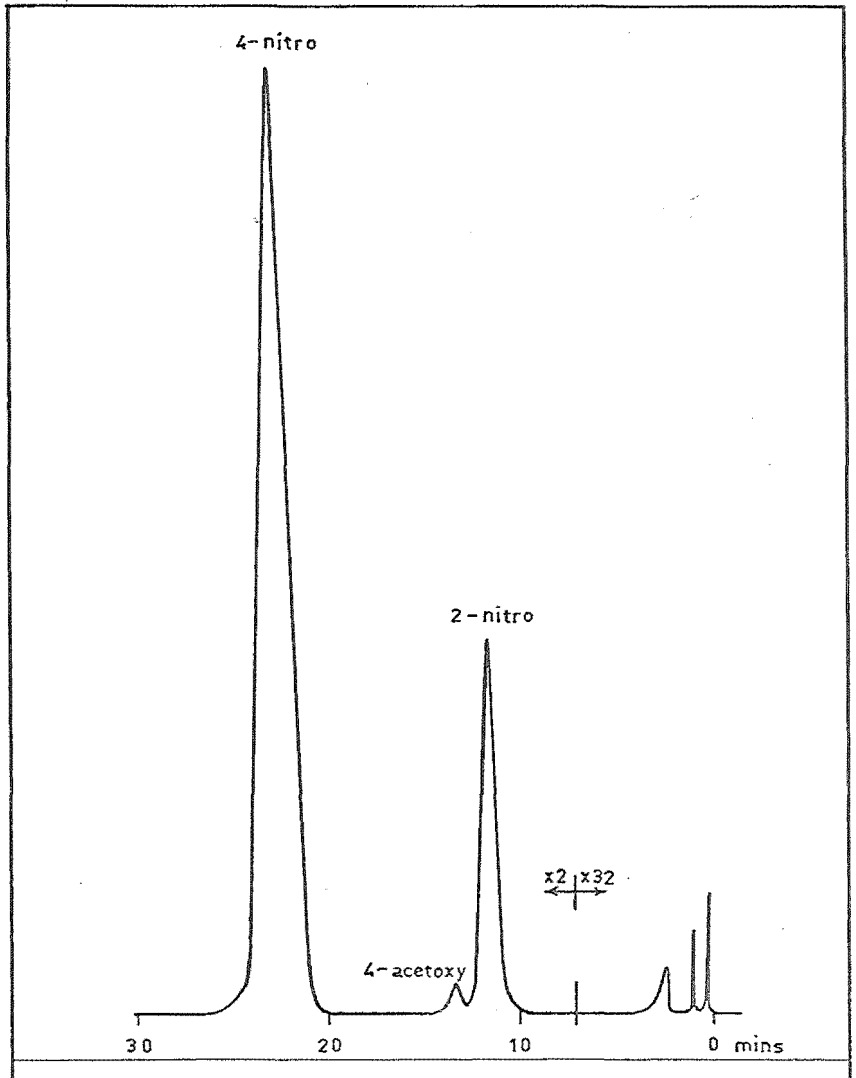


FIG. 5 m-Xylene - Ac_2O

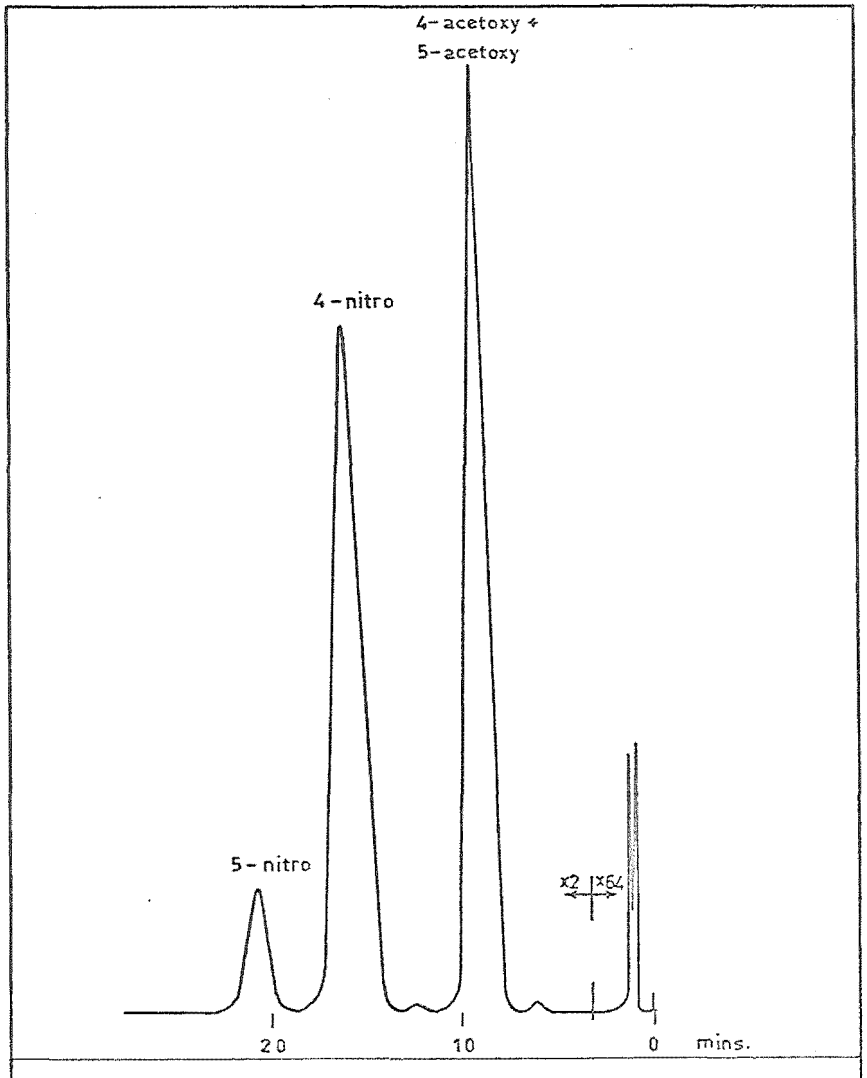


FIG. 6 Hemimellitene - Ac_2O

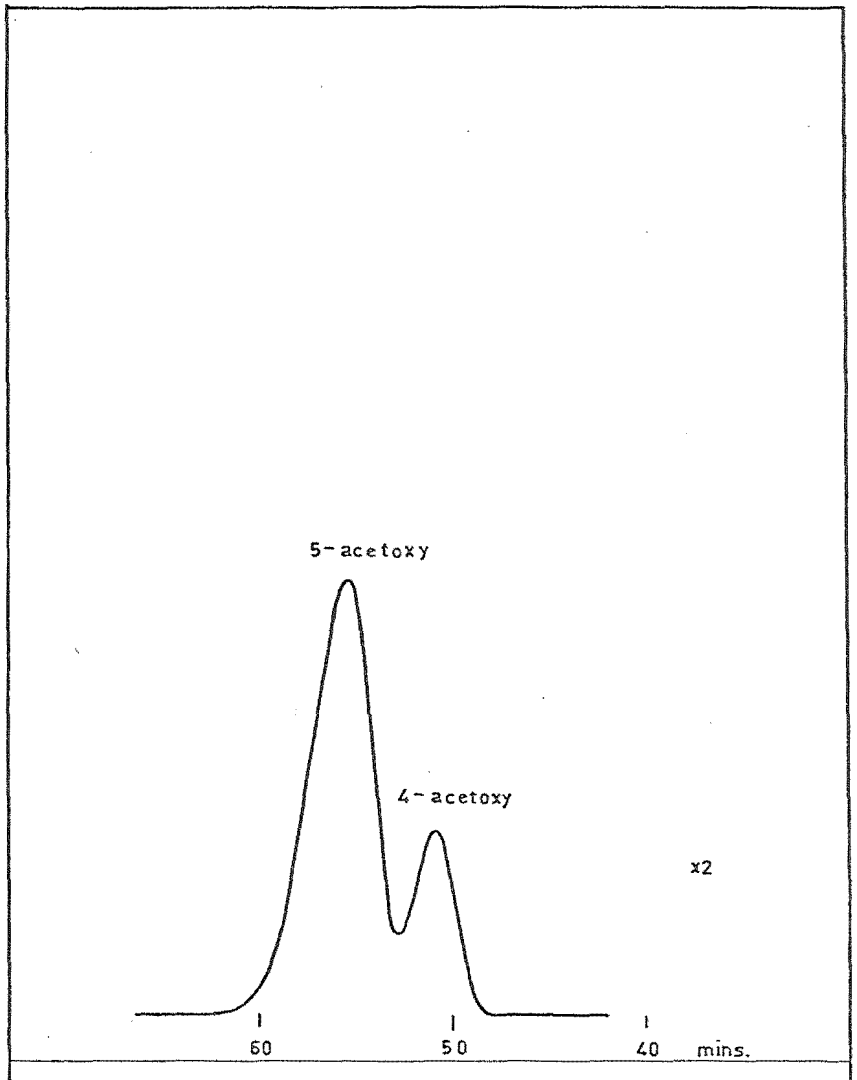


FIG. 7 Hemimellitene - Ac_2O (series 2)

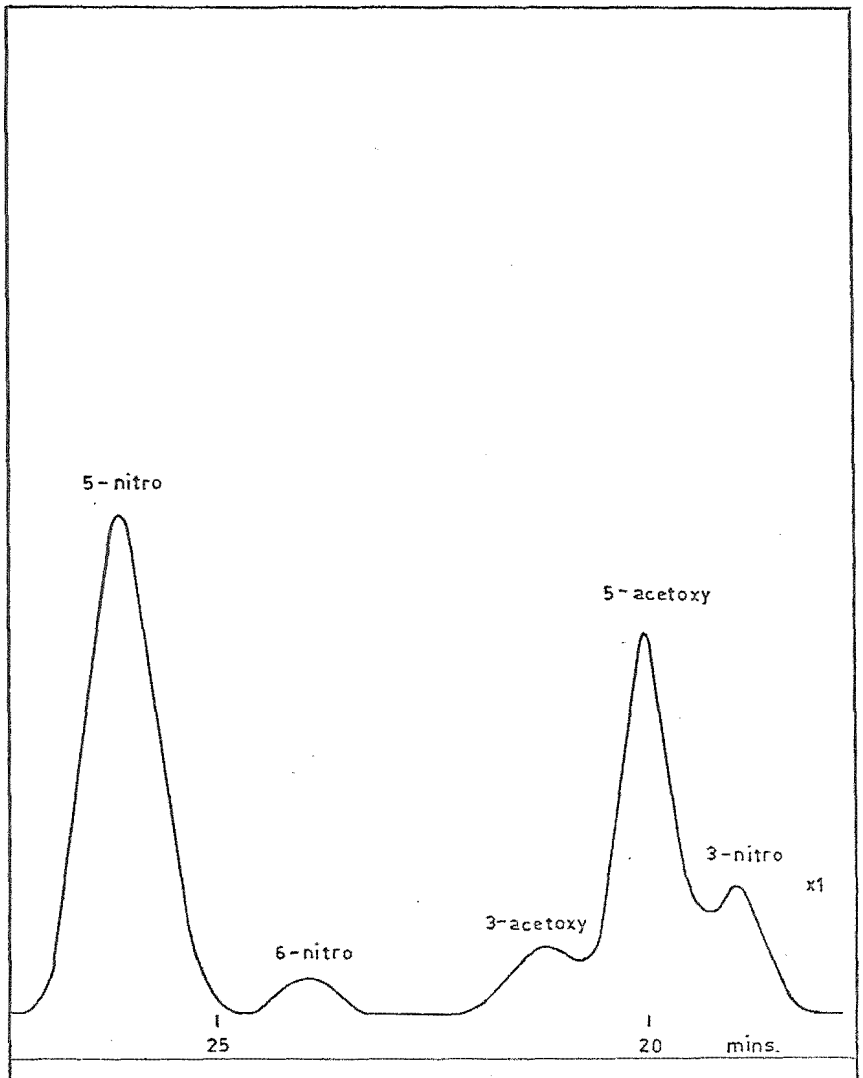


FIG. 8 Pseudocumene - Ac_2O (Megachrom)

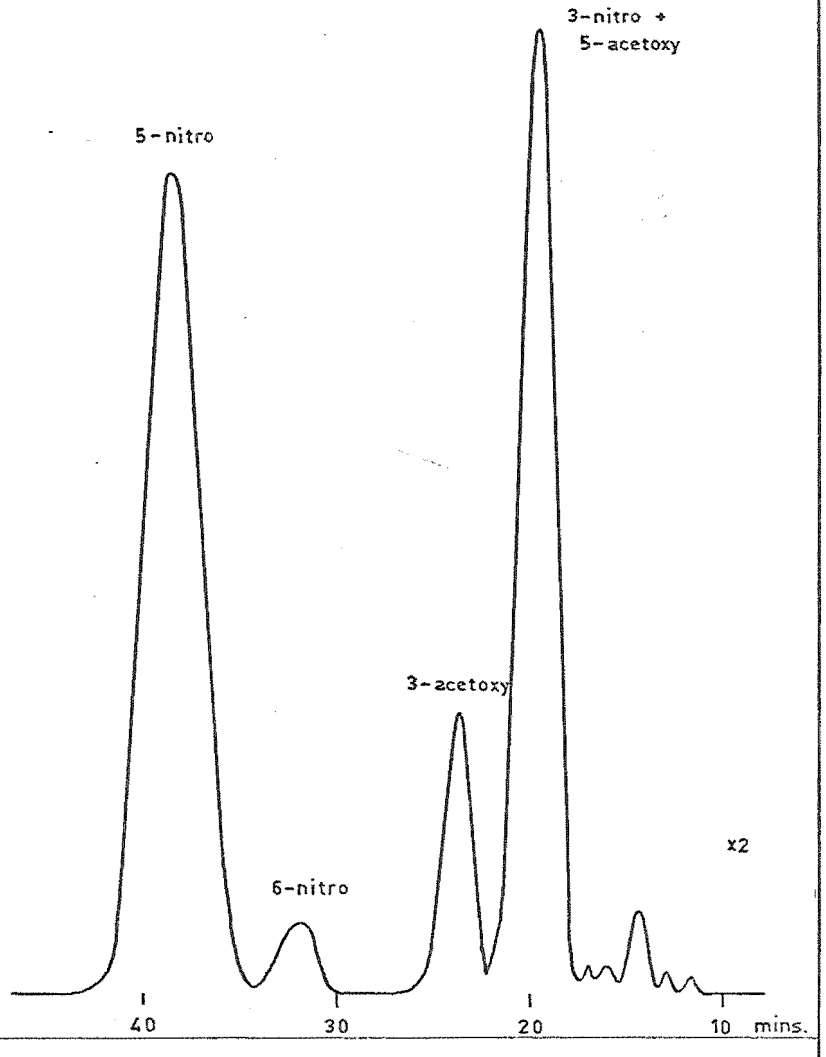


FIG. 9 Pseudocumene - Ac_2O

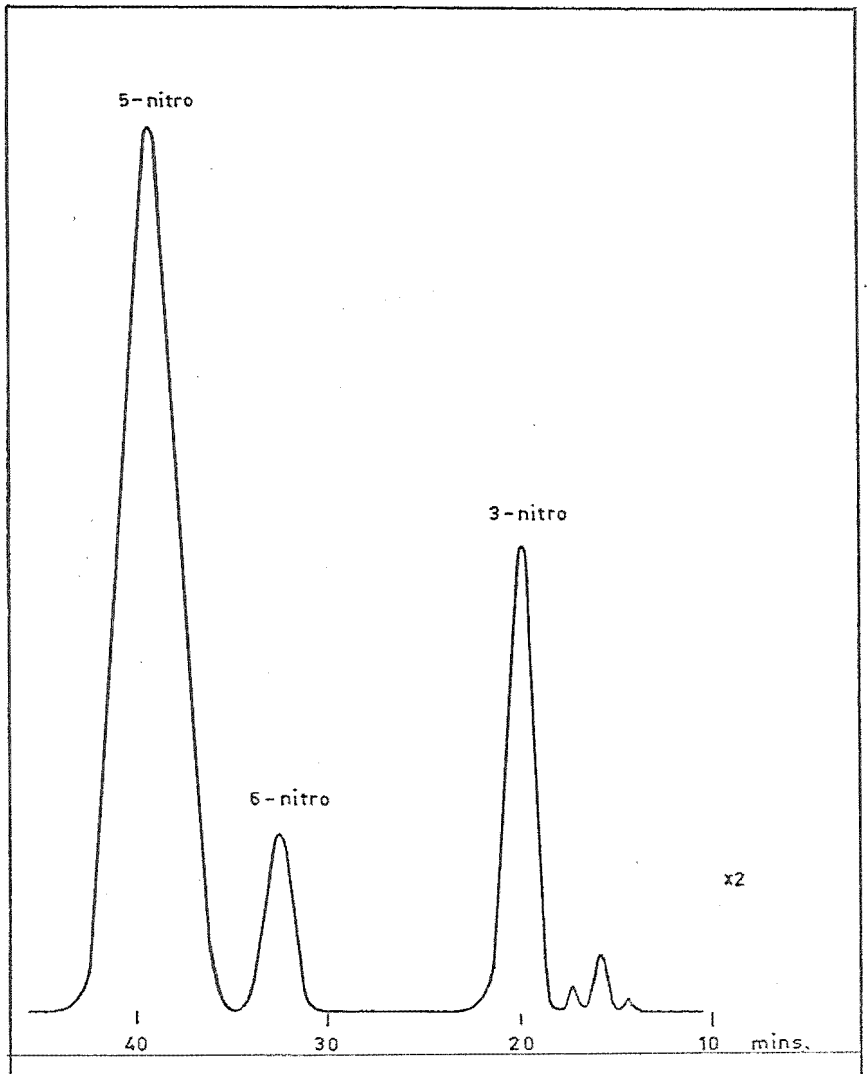


FIG. 10 Fig.9 after hydrolysis

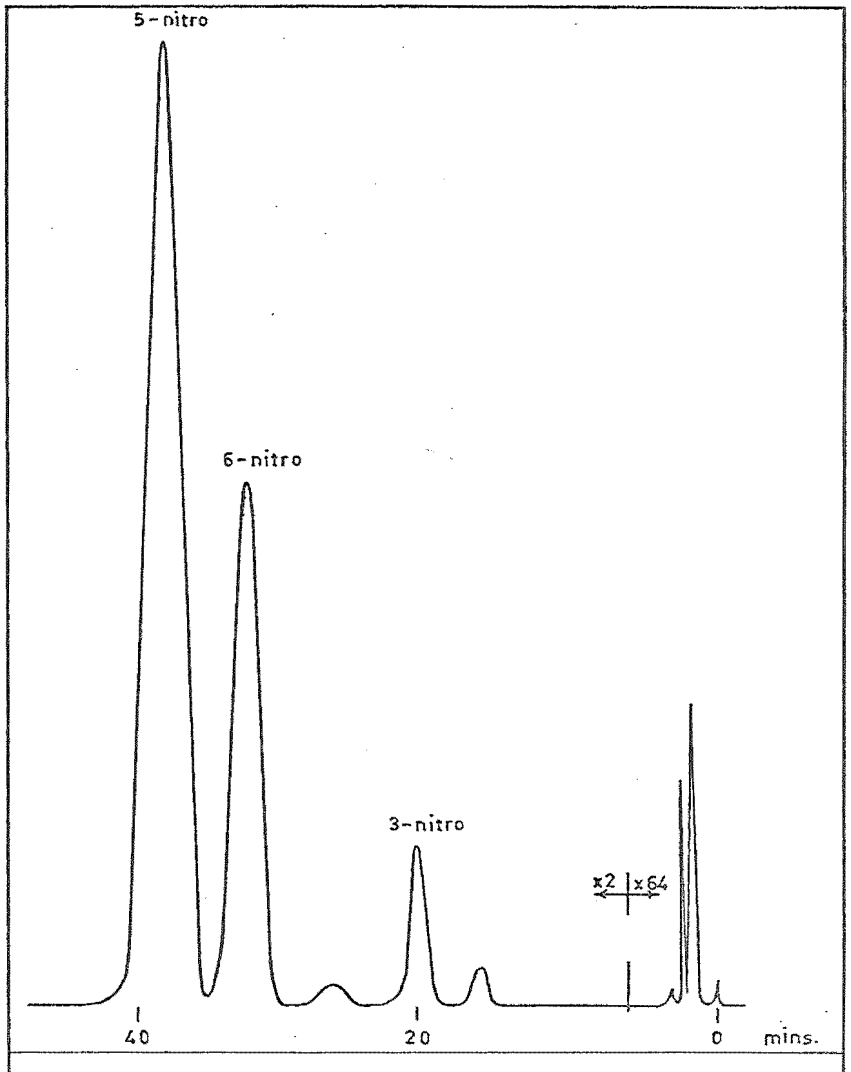


FIG. 11 Pseudocumene - $MeNO_2$

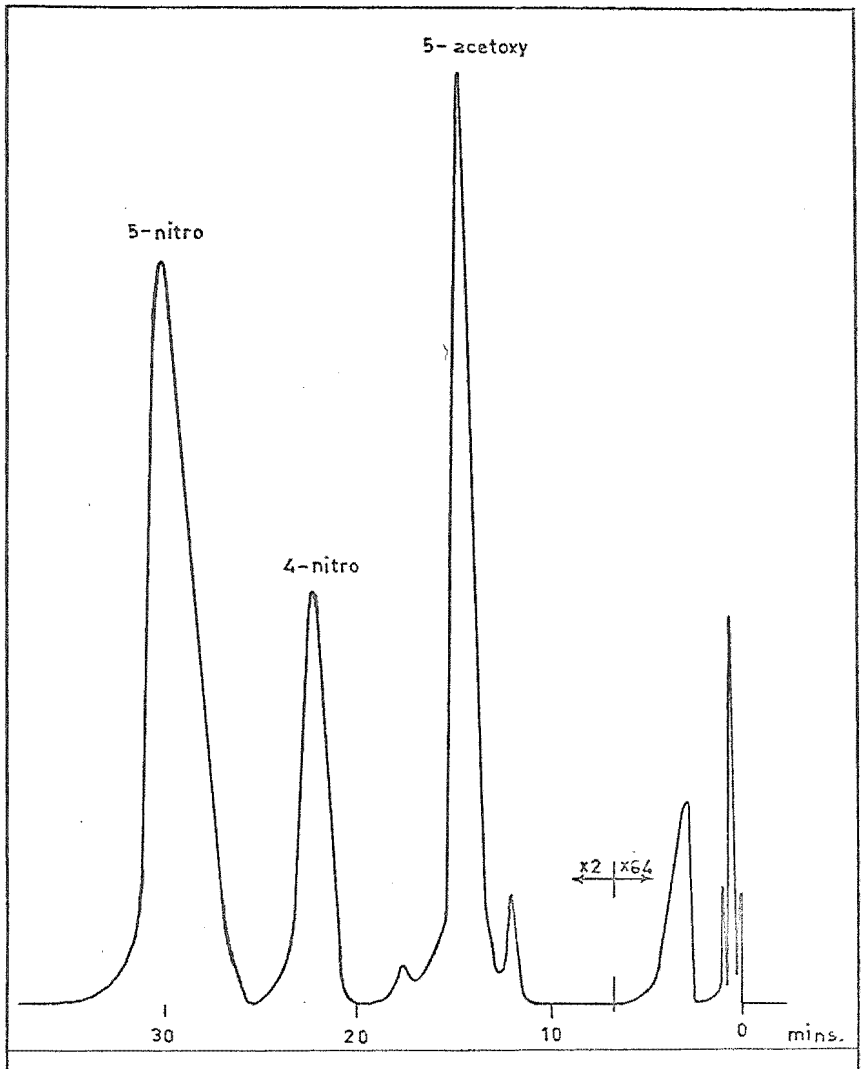


FIG. 12 Indan - Ac_2O

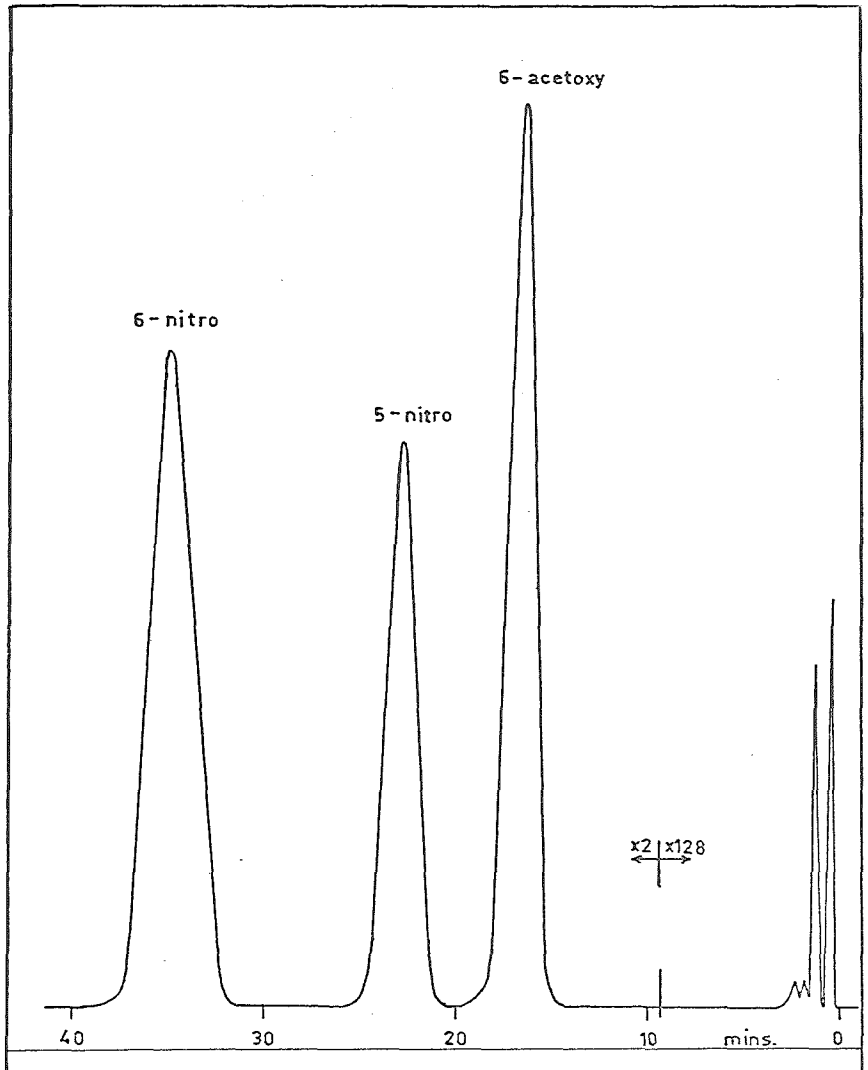


FIG. 13 Tetralin - Ac_2O

DISCUSSION

Composition of the Reaction Mixtures

(a) Nitric acid-acetic anhydride mixtures

The final stoichiometric composition of the reaction mixtures used was: hydrocarbon, 0.008 moles approximately; nitric acid, 0.0048 moles; acetic anhydride, 0.032 moles. The composition of the nitrating mixture made up for addition to the hydrocarbon solution was; nitric acid, 0.0048 moles; acetic anhydride, 0.011 moles. At all times, therefore, the hydrocarbon was in at least twofold excess over nitric acid, and the mole ratio of nitric acid to acetic anhydride was not greater than 0.44. The formation of acetyl nitrate should therefore be favoured (see Introduction, p. 23) and polynitration be reduced to a minimum. Table XXII (p. 103) shows that between 70% and 90% of the nitric acid used can be accounted for as either nitro- or acetoxy-product. Some nitric acid is lost from the solutions because of its high vapour pressure. It seems unlikely therefore that significant polynitration occurs. No high-boiling materials could be detected from these reactions on the gas chromatograph, and careful distillation of the o-xylene reaction product under vacuum gave only a small amount of residue in the still pot, amounting to about 1-3% of the total product.

(b) Nitronium tetrafluoroborate-sulpholane mixtures

The final stoichiometric composition of these mixtures was: sulpholane, 0.074 moles; NO_2BF_4, 0.0012 moles; hydrocarbon, 0.008 moles approximately. The hydrocarbon was in at least sevenfold excess over the nitronium salt. A comparison of Olah's reaction mixtures and those used in this work is given below (for equal moles of hydrocarbon):

Reagent	Olah et al.[20]	This work
hydrocarbon	0.5	0.5 moles
NO_2BF_4	0.05	0.072 moles
sulpholane	1.08	6.5 moles

Under his conditions Olah found no evidence for poly-nitration, and obtained a 98% material balance on a preparative scale by fractionation of the product. The products obtained from the reactions at the lower concentrations used in this work showed no trace of higher-boiling materials on the gas chromatograph, and no significant residue was obtained on vacuum distillation of the material.

(c) Nitric acid-nitromethane mixtures

The final stoichiometric concentrations used were: hydrocarbon, 0.0083 moles approximately; nitric acid, 0.024 moles; nitromethane, 0.13 moles; sulphuric acid, 0.0004 moles. The use of more than the hydrocarbon

equivalent of nitric acid is necessary in this system to obtain sufficient reaction in a limited time. Since the nitric acid solution is added to the hydrocarbon solution slowly, the actual concentration of nitric acid present in the mixture during the course of the reaction is much less than the total quantity used. The sulphuric acid concentration used (0.03M) was the minimum concentration which would give a useful quantity of product in the $1\frac{1}{2}$ hours reaction time. No polynitro compounds could be detected in the products of reactions in these solutions, either on the gas chromatograph or by distillation.

The Acetoxylation Reaction

(a) The reaction products

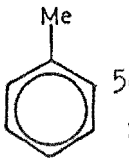
The reaction of o-xylene with nitric acid in acetic anhydride gives the expected two nitro-o-xylenes. In addition, 3,4-dimethylphenyl acetate is produced as 58% of the total product. Further investigation showed that this acetate is formed in reproducible amounts (Table XXIV) and that no other product, either isomeric acetate or acetoxy nitroxylene is produced. The two nitro-o-xylenes remain unchanged after treatment with nitric acid in acetic anhydride under the reaction conditions. The acetate must therefore be produced from reaction of the hydrocarbon with the acid-solvent system.

Acetoxylation was found to occur with each of the hydrocarbons studied. Table XLIV summarises the product ratios obtained under the standard conditions. Because this direct acetoxylation of aromatic hydrocarbons had not been previously reported, a brief study of the reaction was undertaken.

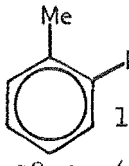
TABLE XLIV

Product distributions from nitration in nitric acid-acetic anhydride mixtures

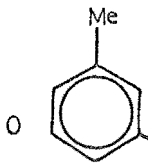
All figures are mole percentages. Figures in brackets are acetoxy product, those outside are nitro products.



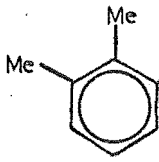
58·2 (0)
2·8 (0)
35·9 (3·1)



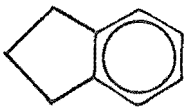
13·5 (0)
28·0 (58·6)



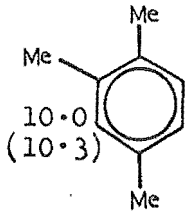
14·7 (0)
0
84·7 (0·7)



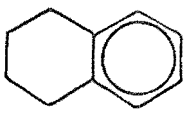
46·4 (10·6)
7·7 (35·3)



51·5 (30·2)
18·2 (0)



4·3 (0)
10·0
(10·3)
49·7 (25·6)



44·2 (32·0)
23·9 (0)

(b) The nature of the reaction

The results of experiments described in this and subsequent sections are summarised in Tables XLV and XLVI.

Free radical attack of the hydrocarbon under the conditions used is unlikely to occur, but the possibility of acetoxylation occurring in this way was tested by treating o-xylene with diacetyl peroxide in acetic anhydride. No acetoxy-o-xylene was obtained. The product distributions obtained (Table XLIV) strongly suggest an electrophilic attack to form the acetoxy products.[142,143] The proportion of acetoxylation increases as the activity of the substrate towards electrophilic attack increases, but the acetoxylation is subject to greater steric hindrance than is nitration. Toluene gives about 3% para-acetoxy product only. o-Xylene, with both positions more highly activated than toluene, gives nearly 60% acetoxy product in the 4-position, but none in the 3-position which is hindered by a "buttressed" methyl group.[88] In m-xylene only the 5-position, meta to both methyl groups, is unhindered. The 2- and 4- positions are highly activated but only a trace of acetoxy is found in the less hindered 4-position. In hemimellitene the 4-positions are more activated (o, m, and p-methyl) than the 5-position (m, m, and p-methyl), but the 5- position gives 35% acetoxy product and each 4-position 5%. This is explained by the considerable steric hindrance

TABLE XLV

Product distribution from the reaction of o-xylene with nitric acid-acetic anhydride at 0°. Changes in reactant concentrations and addition of other reagents

	[o-xylene]$^{+}$ (mole l^{-1})	[HNO_3]$^{+}$ (mole l^{-1})	[Other reagents] (mole l^{-1})	Product analysis A	B	C	Acetoxy-/Nitro- ratio
*	2.73	1.6	--	56.7	14.0	29.4	1.31 ± 0.05
	2.0	1.6	--	56.2	14.9	28.9	1.29 ± 0.05
	4.1	1.6	--	56.8	15.0	28.3	1.31 ± 0.05
	5.6	1.6	--	57.8	13.3	29.0	1.37 ± 0.05
	2.73	0.2	--	55.8	14.8	29.4	1.26 ± 0.05
	2.73	2.4	--	55.8	13.5	30.7	1.26 ± 0.05
	2.73	1.6	H_2SO_4, 0.016	58.2	14.3	27.6	1.40 ± 0.06
	2.73	1.6	H_2SO_4, 0.032	62.4	12.2	25.5	1.66 ± 0.06
	2.73	1.6	AcOH, 3.0	55.2	14.6	30.3	1.24 ± 0.05
	2.73	1.6	AcOH, 6.2	56.7	13.9	29.4	1.31 ± 0.05
	2.73	--	H_2SO_4, 1.1	no reaction			--
	2.73	--	H_2SO_4, 1.6 Acetyl peroxide 1.6	no reaction			--

* Standard reaction. + Concentrations in moles/litre of Ac_2O present in final mixture.

A = %4-acetoxy- B=%3-nitro- C=%4-nitro-o-xylene

TABLE XLVI

Variation with time of the acetoxy:nitro product ratio in the nitration of o-xylene in nitric acid-acetic anhydride at 0°

Reaction time (minutes)	Product percentages			Acetoxy:nitro ratio
	A	B	C	
15	56.7	14.0	29.4	1.31
30	55.8	14.2	29.9	1.27
60	56.2	14.0	29.8	1.29
90	55.8	14.2	30.0	1.26
120	58.3	13.0	28.8	1.40

A = 4-acetoxy B = 3-nitro C = 4-nitro

at the 4-position resulting from the adjacent "double-buttressed" methyl group.[88] The 5-position in pseudocumene is activated by o, m, and p-methyl groups as is the 4-position in hemimellitene, but the former is hindered only by an isolated methyl group and gives 25% acetoxy product. Indan and tetralin might be expected to be similar to o-xylene, and both give no acetoxy product adjacent to the fused saturated rings, but appreciable amounts at the 5- and 6-positions respectively.

(c) Kinetic evidence

Since the completion of this section of the work, Read has investigated the kinetics of the reaction of o-xylene in nitric acid-acetic anhydride mixtures under conditions similar to those used here.[42,144] Read found that both the nitration and acetoxylation reactions are zeroth order in o-xylene, and that the ratio of the rates of acetoxylation and nitration is constant during the reaction. Added acetic acid, sulphuric acid or lithium nitrate have no effect on the rate ratio. These results agree with studies made in this work. Table XLV shows that the product distribution obtained in this reaction, and the acetoxy:nitro product ratio, is independent of hydrocarbon concentration, nitric acid concentration, added sulphuric acid and added acetic acid over the concentration ranges tested. Table XLVI shows that the acetoxy:nitro

product ratio is independent of the reaction time. Also, since sulphuric acid-acetic anhydride mixtures do not acetoxylate (Table XLV), the acetoxylating species cannot be protonated acetic anhydride. Read concludes from these facts and from a detailed analysis of his kinetic results that the same species is responsible for both acetoxylation and nitration, and that this species is one of the three possible protonated acetyl nitrates. The mechanism is

$$HNO_3 + Ac_2O \rightleftharpoons AcO.NO_2 + AcOH$$

$$AcO.NO_2 + HA \rightarrow AcO.NO_2\,H^+A^- \qquad \text{(slow)}$$

$$ArH + AcO.NO_2,H^+A^- \xrightarrow{\text{fast}} \begin{cases} ArOAc + HNO_2 + HA \\ ArNO_2 + AcOH + HA \end{cases} \qquad \text{(fast)}$$

It should be noted that this mechanism requires the formation of one mole of nitrous acid for every mole of acetoxy product formed. Nitrite is produced during the reaction and can be detected using a modified Griess-Ilosvay test. Quantitative measurements (p. 102 and Table XXII) showed that about 60% of the theoretical amount of nitrite could be accounted for. Since nitrous acid decomposes in acid solution[145] it is likely that during the course of the reaction some nitrite will be lost from the solution, explaining both the low value for total nitrite produced and the variations in the results obtained.

An important consequence of the above mechanism is that different hydrocarbons should give different acetoxy:

nitro product ratios, since this ratio is determined by competition between two positions of the protonated acetyl nitrate for the hydrocarbon. Read showed that o-xylene and m-xylene give very different ratios. The results of this work, (Table XLIV) show clearly that the ratio depends on the hydrocarbon used.

(d) Hammett Rho for acetoxylation

Comparison of the ratios of nitration to acetoxylation in the completely unhindered positions of the hydrocarbons studied shows that the species responsible for acetoxylation is more selective, and therefore less active, than the nitrating species; i.e., the Hammett rho value for acetoxylation is larger than that for nitration.

Substrate	Position	Activation	Nitro:acetoxy ratio
toluene	4-	p-Me	11.6
o-xylene	4-	m, p-Me	0.52
hemimellitene	5-	m, m, p-Me	0.22

Although only three such unhindered positions are available, an estimate of the value of rho for acetoxylation is possible by assuming that to a first approximation the Additivity Principle is valid for o-xylene and hemimellitene. For any given position in the hydrocarbon ArH the following equations hold:

$$ArH + R_N \xrightarrow{k_N} N \text{ (nitro product)}$$

$$ArH + R_A \xrightarrow{k_A} A \text{ (acetoxy product)}$$

$$N/A = \frac{dN}{dt} \cdot \frac{dt}{dA} = k_N R_N / k_A R_A$$

Since the nitrating and acetoxylating species are the same

$$N/A = k_N/k_A$$

For a polymethylbenzene, $\log k/k_o = \rho \sum_i \sigma_i^+$ (see p. 37)

Thus $\log k_N/k_N^o = \rho_N \sum_i \sigma_i^+$

$$\log k_A/k_A^o = \rho_A \sum_i \sigma_i^+$$

Whence by subtracting and rearranging

$$\log k_N/k_A = \log N/A = \log k_N^o/k_A^o + (\rho_N - \rho_A)\sum_i \sigma_i^+$$

From this equation, a plot of $\log N/A$ vs $\sum_i \sigma_i^+$ should have slope $(\rho_N - \rho_A)$ and intercept $\log\left(N/A\right)_{benzene}$.

The completely unhindered positions are either <u>meta</u> or <u>para</u> to the methyl groups, and Brown's $\sigma^+_{\underline{p}\text{-Me}}$ and $\sigma^+_{\underline{m}\text{-Me}}$ values of -0.278 and -0.079 may be used to evaluate $\sum_i \sigma_i^+$ for each position.[146] It will be shown later that a value of $\rho_N = -7.1$ for nitration in nitric acid-acetic anhydride mixtures may be obtained from the nitro product distributions in this system. (Brown's mean value for nitration is -6.2).[145] Use of this value enables ρ_A to be calculated

from ($\rho_N - \rho_A$). The three points are plotted on the graph. (Fig. 25, p. 148) The values of ρ_A obtained from the lines shown are -25, -12, and -18, giving a mean value of -18. This graph is in effect an attempt to investigate a Hammett plot over a very narrow range of reactivities, and the very wide spread in values is not surprising, particularly as the values on the reactivity scale are calculated assuming the Additivity Principle to be valid. It seems likely however, that the value of ρ_A is much larger than ρ_N; this, coupled with the considerable steric requirements of the acetoxylation reaction would be sufficient to explain the product distributions obtained. The intercept of the graph must lead to a ratio of $^N/_A$ for benzene which is very large, since no acetoxy product can be detected. This lends weight to the high values of ρ_A.

The high value of ρ_A implies that bond formation in the transition state is further advanced in acetoxylation than it is in nitration; i.e., the transition state in acetoxylation lies closer to the σ-complex than it does in nitration. C-O and C-N bond lengths are very similar[147] (1.42 and 1.47Å respectively) and thus the acetoxylation reaction would be expected to be more readily susceptible to steric hindrance than nitration, as found.

Hammett rho for acetoxylation

$\log\frac{N}{A}$ vs. $\Sigma\sigma^+$

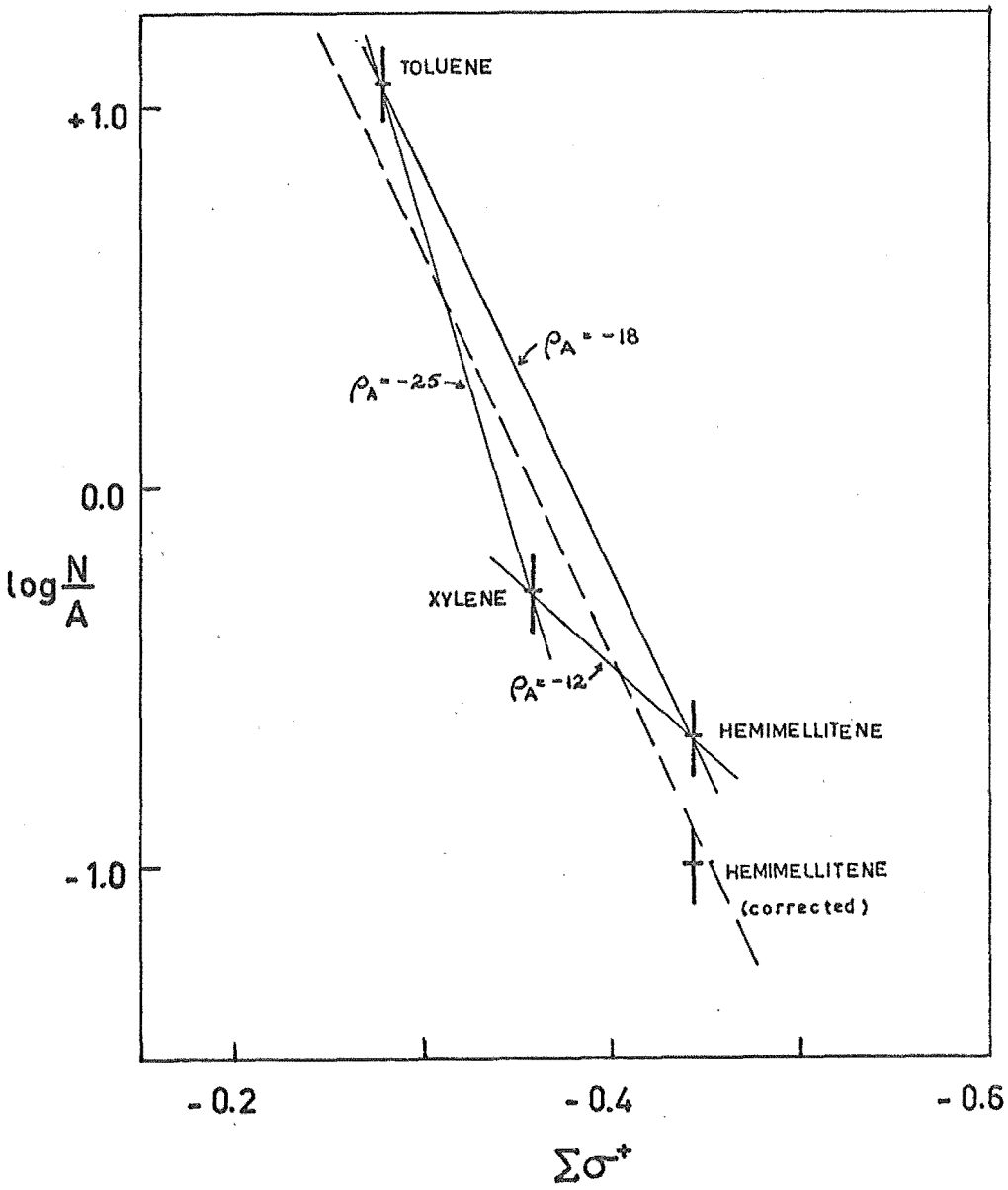
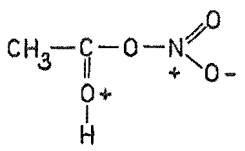


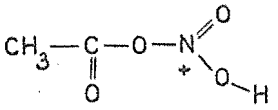
FIG. 25

(e) The structure of the protonated acetyl nitrate

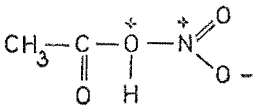
Protonation of acetyl nitrate may occur at the carbonyl oxygen, at a terminal nitro-oxygen atom, or on the central oxygen atom to give the three species I, II and III. Protonation of the central oxygen should be more difficult



I



II



III

than at the other two positions since it is flanked by two powerful -I-M groups. The carbonyl oxygen is likely to be more readily protonated than the nitro- oxygens by analogy with the relative acid strengths of benzoic acid ($pK_a = -7.26$) and nitrobenzene ($pK_a = -11.38$). Thus the order of ease of formation, which will be the reverse of the order of reactivity if the transition states for the reaction are assumed to be similar, is I > II > III. Further, structure I has more resonance stabilisation than II or III, and III is further destabilised by carrying formal positive charges on adjacent atoms.

The rate-determining formation of the protonated acetyl nitrate responsible for acetoxylation and nitration, suggested both by the results of this work and by Read's

kinetics, makes species III the most likely electrophile in these reactions, since it is the slowest in forming. However this species, with a formal positive charge on the central oxygen, would be expected to show low selectivity in acetoxylation in common with reactions such as mercuration and isopropylation which involve attack by highly polar species. This objection is not too serious, as the positive charge must be considerably spread by resonance. However, species II should be a much more effective nitrating agent than species III and is formed more rapidly; nitration might therefore be expected to be brought about by species II. If this is so, acetoxylation must also occur through this species.

Species II might be expected to be a more reactive nitrating than acetoxylating species, with consequently greater selectivity in acetoxylation than nitration. Species I might be expected to show these characteristics to a lesser extent, but acetoxylation by S_N2' attack on the carbonyl oxygen of this species seems unlikely since such attack would suffer little steric hindrance. No final selection between the three possible species can be made on the results of this work.

A number of other points are pertinent to this problem. It is essential to Read's argument that o-xylene and m-xylene react at the same total rate—the rate of

formation of the reactive species. In fact he found that m-xylene reacted slightly faster than o-xylene, that the rate depended slightly on the concentration of m-xylene and that the acetoxylation:nitration rate ratio decreased slightly as the m-xylene concentration increased. Read found that by assuming a second mode of nitration, first order in substrate and available to m-xylene but not o-xylene, by a species which could not produce acetoxylation, he could obtain corrected rate constants for the zeroth order reaction identical with the values for o-xylene. The corrected acetoxylation:nitration rate ratio for m-xylene was constant. These results are readily explained; m-xylene is a much more reactive substrate than o-xylene (e.g., Table XI) and might be expected to by-pass the rate-determining formation of the most reactive electrophile and react with a more rapidly formed but less reactive species in a rate-determining bimolecular step. Anisole, a more reactive substrate than m-xylene,[83,98] should be more effective in by-passing the zeroth order nitration. Yoong[148] showed that the kinetics of nitration of anisole in nitric acid-acetic anhydride mixtures could be explained in terms of competing zeroth and first order reactions. The rate of the zeroth order nitration was very close to the value found for o-xylene under similar conditions. Yoong considered that the most reactive form of protonated acetyl

nitrate (species III) was responsible for the zeroth order reaction, and that the first order reaction was brought about by species II. Species II is less likely to bring about acetoxylation than species III, a necessary assumption in interpreting the m-xylene kinetics, but anisole should give appreciable yields of acetoxy product by reaction with species III. No such product has been detected, although Yoong did not investigate the reactions at very low anisole concentrations, conditions most favouring the zeroth order reaction.

Diphenylamine reacts about fifty times as fast as the total rate of acetoxylation and nitration of o-xylene in nitric acid-acetic anhydride mixtures.[149] It is unlikely therefore that the protonated acetyl nitrate responsible for reaction with o-xylene makes a significant contribution to the reaction with diphenylamine. Dickson interpreted his kinetic studies of this substrate[149] in terms of a zeroth order reaction with species II and a first order reaction with species I. No acetoxylation could be detected. Diphenylamine is thus sufficiently reactive to by-pass completely the slow formation of species III, and to make the formation of species II rate-determining.

If these conclusions are correct, o-xylene and less reactive hydrocarbons must react with species III to produce both acetoxy and nitro products. The two unexplained

problems in such a view are the absence of acetoxy product from the reaction of anisole, and the apparently rather high selectivity of $Ac\overset{+}{O}H.NO_2$ in acetoxylation.

(f) The ortho:para ratio for nitration in nitric acid-acetic anhydride

Hemimellitene and pseudocumene have reactivities towards electrophilic attack similar to that of m-xylene.[98] These substrates must therefore also undergo nitration by the species responsible for the first order nitration of m-xylene, but substrates of reactivity similar to or less than that of o-xylene (e.g., indan and tetralin) should not be attacked by this species. Read has shown that the nitration of toluene in these systems is mixed first and zeroth order in substrate, in keeping with a bimolecular reaction between substrate and protonated acetyl nitrate of about the same rate as the formation of the protonated species. This does not affect the comparison of ortho:para ratios derived from toluene with those from o-xylene, indan or tetralin, since the same attacking entity is involved in all cases. However, the incursion of a second protonated acetyl nitrate into the reaction of more active substrates presents problems in comparing isomer distributions of these substrates with those derived from toluene.

The species responsible for the first order nitration must be less active than the species responsible for the

zeroth order reaction, and therefore more selective, since the former only becomes important for more active substrates. Ortho:para ratios for the active substrates may therefore bear little relationship to those for toluene and o-xylene. This problem is discussed in the next section.

For his m-xylene runs Read assumed that the total rate of nitration $k_N^1 = k_N + k_N^*[ArH]$ where k_N^* is the pseudo rate constant for the first order nitration and k_N is the rate constant for the zeroth order reaction. He obtained the values

$$k_N = 7.0 \times 10^{-3} l^2 m^{-2} sec^{-1}$$

and

$$k_N^* = 6.2 \times 10^{-3} l^3 m^{-3} sec^{-1}$$

at [ArH] = 0.3M. These values give the fraction of the total nitration rate made up by the first order reaction $\left(k_N^*[ArH]/k_N^1\right)$ as about 14%. If it is assumed that these rate constants hold at the higher hydrocarbon concentrations used in this work (2.5M) this figure becomes 54%, and if it is further assumed that this value is roughly true for hemimellitene in the 5-position, the nitro:acetoxy ratio for this position (0.22) becomes 0.10 for nitration by the acetoxylating species alone. Use of this value in the plot of log N/A (Fig. 25) gives the fourth point shown on the graph; although this calculation is extremely approximate, it lends weight to the higher values of ρ_A obtained. No

matter what the magnitude of the change in the value of N/A, it would always be such as to move this point in the same direction.

The Additivity Principle

In this section, the application of the Additivity Principle to the calculation of product distributions in the methylbenzenes is discussed. The results obtained in the three nitrating systems are taken together; the problem arising from the first order nitration of active hydrocarbons in nitric acid-acetic anhydride mixtures (see p. 153) is discussed at the end of the section. The results are summarised in Tables XLVII to XLIX.

(a) Product distributions in nitric acid-acetic anhydride mixtures

The product distributions used for this nitration system are those for the nitration reaction only, (Table XLVII). Although nitration and acetoxylation occur through the same electrophile, the following analysis shows that the two reactions must be considered separately when comparing product distributions. For reaction at positions 1 and 2 of any given hydrocarbon, the rates of acetoxylation and nitration relative to one position in benzene are:

Position 1: $k_A^1 = 10^{\rho_A \Sigma_1 \sigma}$ $\quad k_N^1 = 10^{\rho_N \Sigma_1 \sigma}$

Position 2: $k_A^2 = 10^{\rho_A \Sigma_2 \sigma}$ $\quad k_N^2 = 10^{\rho_N \Sigma_2 \sigma}$

Thus the ratio of total product (A+N) at position 1 to that at position 2 is

$$k^1_A + k^1_N / k^2_A + k^2_N = 10^{(\rho_A + \rho_N)\Sigma_1\sigma} / 10^{(\rho_A + \rho_N)\Sigma_2\sigma}$$

Clearly, such a ratio bears no simple relationship to the sums of the sigma values at the two positions. On the other hand, the ratios of either the nitro products

$$k^1_N / k^2_N = 10^{\rho_N(\Sigma_1\sigma - \Sigma_2\sigma)}$$

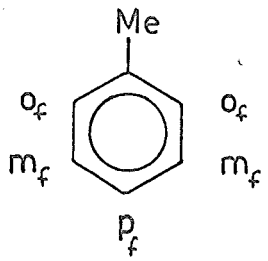
or the acetoxy products

$$k^1_A / k^2_A = 10^{\rho_A(\Sigma_1\sigma - \Sigma_2\sigma)}$$

are simply related to the $\Sigma\sigma$ values, a necessary condition for the application of the Additivity Principle. Many of the hydrocarbons studied undergo acetoxylation at only one position and the acetoxy product ratios cannot be used. The ratios of the nitro products are therefore used in this section.

(b) Toluene

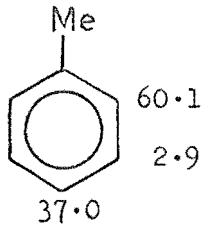
The rates of substitution at each position in toluene relative to one position in benzene are

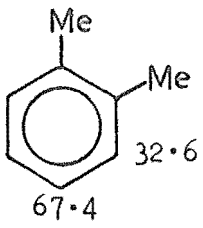


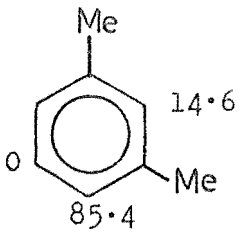
(Ctd. p.161)

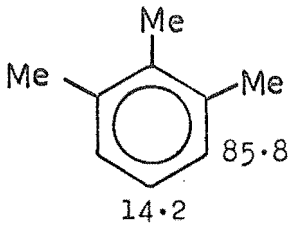
TABLE XLVII

Product distributions: nitric acid-acetic anhydride mixtures
Percentage of total nitro product









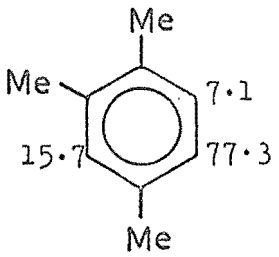
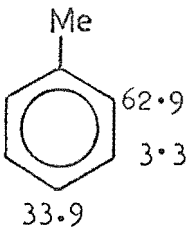
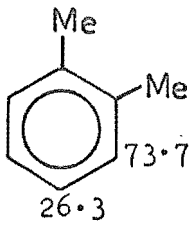
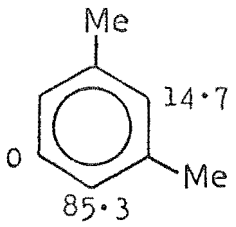


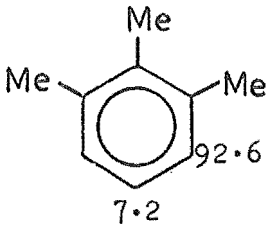
TABLE XLVIII

Product distributions: NO_2BF_4-sulpholane mixtures
Percentage of total nitro product









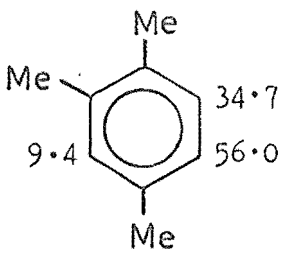
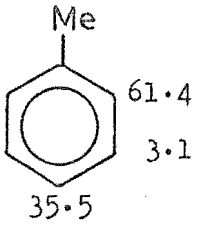
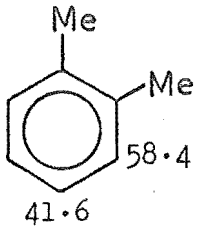
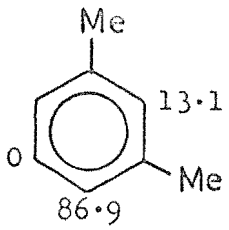


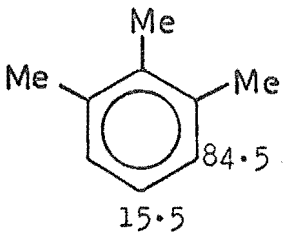
TABLE XLIX

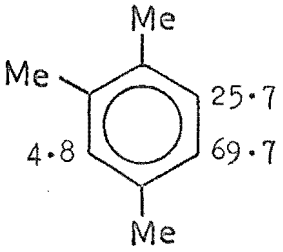
Product distributions: nitric acid-nitromethane mixtures
Percentage of total nitro product











The product ratios are thus $o:m:p = 2o_f:2m_f:p_f$, or

$o : m = o_f : m_f$; $o_f : m_f = o : m$

$p : m = \frac{1}{2}p_f : m_f$; $p_f : m_f = 2p : m$

$o : p = 2o_f : p_f$; $o_f : p_f = \frac{1}{2}o : p$

Using these expressions the partial rate factor ratios for toluene in each system may be calculated (Table L).

TABLE L

Partial rate factor ratios for toluene

Nitrating system	o_f/m_f	p_f/m_f	o_f/p_f
HNO_3-Ac_2O	21 ± 8	26 ± 10	0.81 ± 0.07
NO_2BF_4-sulpholane	19 ± 8	21 ± 10	0.93 ± 0.08
HNO_3-$MeNO_2$	20 ± 4	23 ± 4	0.86 ± 0.03

The ratios in this table are calculated from the most reliable experimental results. For example, the o:p ratio in toluene is calculated from the ortho and para product percentages determined from the chromatograms by measuring the peaks corresponding to these isomers only. (* values in the tabulated results). The very large errors in the o_f/m_f and p_f/m_f values arise from the difficulty in determining the small amount of meta product formed.

(c) Partial rate factor ratios for the polymethylbenzenes

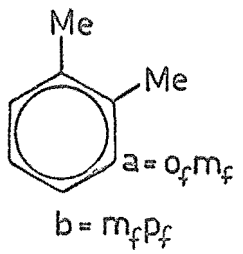
If the Additivity Principle is valid for these compounds, the partial rate factor ratios calculated for toluene should be the same as the values calculated from the

product distributions for the polymethylbenzenes by means of the expressions in Table LI. The ratios calculated from these expressions are listed in Table LII. The values for toluene from Table L are included for comparison. It is clear that there is little or no correlation between the values for toluene and the values for the other hydrocarbons. Although the errors in the ratios involving minor components are large, they are not sufficiently great to account for the differences.

(d) Calculated product distributions

A more satisfactory test of agreement between the predictions of the Additivity Principle and the experimental results is to use the partial rate factor ratios for toluene to calculate the product distributions for the other methylbenzenes. This approach has been used by Brown and Marino[89] to calculate the isomer distributions for the acetylation of m-xylene and hemimellitene. Agreement with experiment was poor, particularly in the case of hemimellitene.

For o-xylene, for example,



$a/b = o_f/p_f = \frac{3\text{-nitro}}{4\text{-nitro}}$;

Total product at a and b = 100%

(Ctd. p.165)

TABLE LI

Equations for partial rate factor ratios

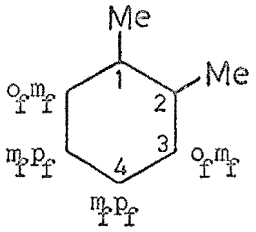
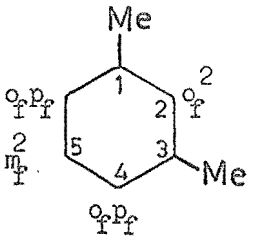
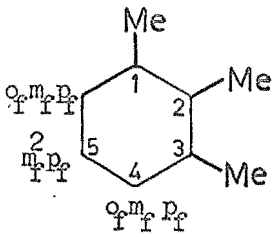
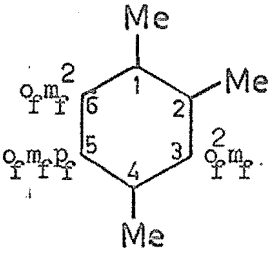
Hydrocarbon	Partial rate factors	Partial rate factor ratios
o-xylene		3-nitro/4-nitro = o_f/p_f
m-xylene		2-nitro/4-nitro = $\frac{1}{2} \cdot o_f/p_f$ 2-nitro/5-nitro = $(o_f/m_f)^2$
hemimellitene		4-nitro/5-nitro = $2o_f/m_f$
pseudocumene		3-nitro/5-nitro = o_f/p_f 5-nitro/6-nitro = p_f/m_f 3-nitro/6-nitro = o_f/m_f

TABLE LII

Partial rate factor ratios for the polymethylbenzenes

(a) Nitric acid-acetic anhydride

Hydrocarbon	o_f/m_f	p_f/m_f	o_f/p_f
toluene	21 ± 8	26 ± 10	0.81 ± 0.07
o-xylene	--	--	0.49 ± 0.05
m-xylene	--	--	0.34 ± 0.03
hemimellitene	3.0 ± 0.3	--	--
pseudocumene	2.2 ± 0.5	11.0 ± 1	0.2 ± 0.02

(b) NO_2BF_4-sulpholane

toluene	19 ± 8	21 ± 10	0.93 ± 0.08
o-xylene	--	--	1.4 ± 0.1
m-xylene	--	--	0.30 ± 0.02
hemimellitene	2.7 ± 0.2	--	--
pseudocumene	0.19 ± 0.05	2.7 ± 0.3	0.07 ± 0.02

(c) Nitric acid-nitromethane

toluene	20 ± 4	23 ± 4	0.86 ± 0.03
o-xylene	--	--	2.8 ± 0.1
m-xylene	--	--	0.34 ± 0.03
hemimellitene	6.4 ± 1	--	--
pseudocumene	0.27 ± 0.06	1.6 ± 0.1	0.17 ± 0.03

Solving these equations, and similar ones for the other hydrocarbons using the partial rate factor ratios for toluene gives the values in Table LIII.

Some of the differences between observed and calculated values can be explained in terms of steric interaction between the methyl groups and the attacking electrophile. For m-xylene, the experimental value for the 2-isomer is about half the calculated value for each nitrating system, and the experimental value for the 4-isomer is correspondingly higher. Since interference between the two methyl groups is unlikely in m-xylene the whole of this difference may be attributed to steric interaction between the electrophile entering the 2-position and the adjacent methyls. Attack at the 4-position is presumably hindered to the same extent as it is in the ortho position of toluene. Brown and Marino's[89] study of the acetylation of m-xylene unfortunately provides no comparison with this work as acetylation yields no 2-product (the calculated value is 0.3%). Olah[33] has determined product distributions for toluene, o-xylene and m-xylene from nitrations in sulpholane and nitromethane using NO_2BF_4 and related species. The figures for toluene from Olah's work have been used to calculate product distributions for o- and m-xylene on the basis of the Additivity Principle; these values are given in Table LIV with Olah's experimental results. Both calculated

TABLE LIII

Calculated product distributions compared with experimental values

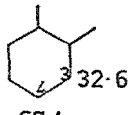
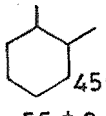
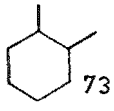
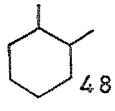
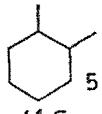
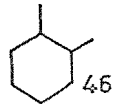
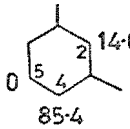
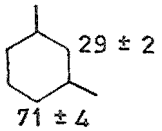
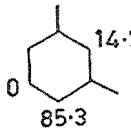
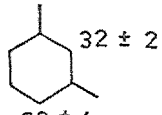
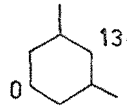
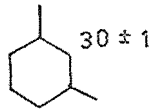
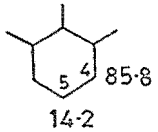
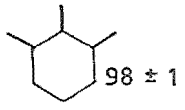
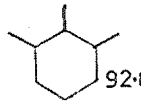
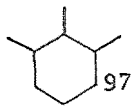
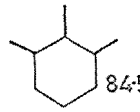
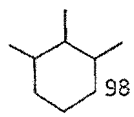
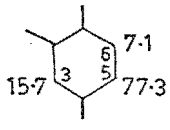
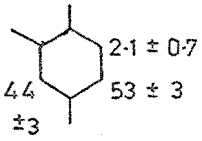
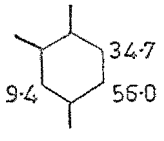
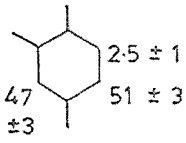
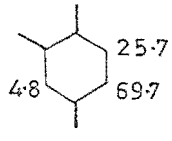
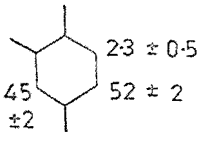
HNO_3-Ac_2O		NO_2BF_4-sulpholane		HNO_3-$MeNO_2$	
Observed	Calculated	Observed	Calculated	Observed	Calculated
 32·6 67·4	 45·±3 55 ± 2	 73·7 26·3	 48 ± 3 52 ± 2	 58·4 41·6	 46 ± 1 54 ± 1
 14·6 0 85·4	 29 ± 2 71 ± 4	 14·7 0 85·3	 32 ± 2 68 ± 4	 13·1 0 86·9	 30 ± 1 70 ± 3
 85·8 14·2	 98 ± 1 2·3 ± 0·4	 92·6 7·2	 97 ± 1 2·6 ± 0·4	 84·5 15·5	 98 ± 1 2·5 ± 0·3
 7·1 15·7 77·3	 2·1 ± 0·7 44 53 ± 3 ±3	 34·7 9·4 56·0	 2·5 ± 1 47 51 ± 3 ±3	 25·7 4·8 69·7	 2·3 ± 0·5 45 52 ± 2 ±2

TABLE LIV

Calculated and experimental product distributions from Olah's work[33]
(Sulpholane as solvent)

A o-Xylene

Nitrating Species	Observed		Calculated	
	%3-nitro	%4-nitro	%3-nitro	%4-nitro
NO_2BF_4	79.7	20.3	48.9	51.1
NO_2ClO_4	77.1	22.9	52.0	48.0
NO_2PtF_6	74.4	25.6	52.0	48.0
NO_2AsF_6	74.8	25.2	51.0	49.0
$NO_2HS_2O_7$	68.7	31.3	47.5	52.5

B m-Xylene

	%2-nitro	%4-nitro	%2-nitro	%4-nitro
NO_2BF_4	17.8	82.2	32.5	67.5
NO_2ClO_4	15.0	85.0	35.5	64.5
NO_2PtF_6	12.4	87.6	35.5	64.5
NO_2AsF_6	12.1	87.9	34.0	66.0
$NO_2HS_2O_7$	14.6	85.4	31.0	69.0

Similar though much less extensive results are obtained in nitromethane as solvent.

and experimental results for m-xylene are very similar to those obtained in this work. In hemimellitene, the observed percentage of 4-nitro product is less than the calculated amount in each system by similar, but not identical, amounts. This difference would be expected because of steric interaction between the electrophile entering the 4-position and the "double-buttressed" methyl group[88] adjacent to it.

Steric interactions of this sort will not explain the results for o-xylene except in the nitric acid-acetic anhydride nitrations, where the hindered 3-position produces less than the calculated amount of product. The difference is not as large as in m-xylene; it seems reasonable that one methyl on each side of the position of attack should be a more effective blocking system than a "single-buttressed" methyl, if only through an entropy effect. However, in the nitric acid-nitromethane and NO_2BF_4-sulpholane systems the percentage of 3-product is greater than the calculated value. Olah's results (Table LIV) show the same effect. Pseudocumene has two hindered positions (3- and 6-) available for attack. The percentage of product formed in the 3-position is only a small fraction of the calculated percentage, as might be expected for a position flanked by a "buttressed" and a single methyl group. The total percentage of 5-and 6-product increases accordingly, but the experimental ratio of 6-product:5-product is higher than the calculated ratio in each system instead of being lowered by steric interaction.

The ratios are shown below.

Nitrating System	Ratio %6-product:%5-product	
	Calculated	Experimental
HNO_3-Ac_2O	0.038	0.091
NO_2BF_4-sulpholane	0.049	0.62
HNO_3-$MeNO_2$	0.044	0.37

The difference between the experimental and calculated ratios is much higher in NO_2BF_4-sulpholane and nitric acid-nitromethane nitrations than in nitric acid-acetic anhydride. The 6-position in pseudocumene is adjacent to a single "buttressed" methyl group, as is the 3-position of o-xylene; it appears that the factor which leads to the high percentage of 3-product in o-xylene is also over-riding the primary steric effect at the 6-pseudocumene position.

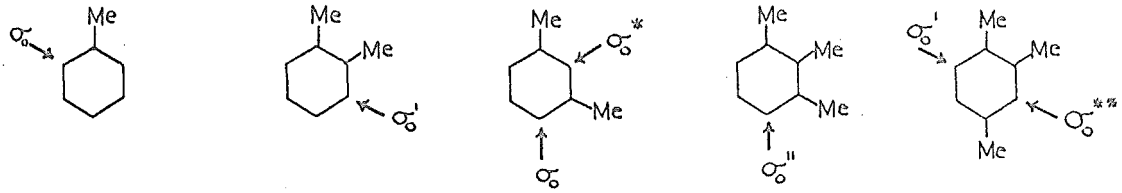
There appears to be no simple explanation for the o-xylene and pseudocumene results in terms of conventional steric and electronic effects. The enhanced reactivity at the positions next to two adjacent methyl groups on the benzene ring is sufficient to overcome the steric hindrance at these positions, but it does not appear to operate in all reactions. It does not occur in o-xylene, and occurs to only a small extent in pseudocumene, in nitric acid-acetic anhydride nitrations. It is not apparent, for example, in the results of Table X (p. 46) taken from the literature. Some investigation of the scope of the effect in other

reaction systems would be of interest.

(e) Modified substituent constants for neighbouring methyl groups

This section attempts to provide a quantitative measure of the effects just described. The contributions made by a methyl group on a benzene ring to the reactivity of the ring in positions meta and para to the methyl group are effectively measured by the $\sigma^{+}_{m\text{-}Me}$ and $\sigma^{+}_{p\text{-}Me}$ substituent constants developed by Brown.[145] The effect of the methyl group on the ortho positions is not necessarily dependent only on the methyl group itself and effective $\sigma^{+}_{o\text{-}Me}$ values cannot be obtained. However, for a given reaction of methylbenzenes under specified conditions, consistent $\sigma^{+}_{o\text{-}Me}$ values are feasible,[150] and this section describes the calculation of such values from the experimental results.

The effect of each methyl group on the ring at its meta and para positions is given by $\sigma^{+}_{m\text{-}Me}$ and $\sigma^{+}_{p\text{-}Me}$ values respectively. The contribution of a methyl group to its ortho position is assumed to depend on the type of ortho position involved. Thus the ortho positions in toluene, adjacent to only one methyl group, are given σ_o values. The other positions adjacent to methyl groups are given the modified σ_o values shown on the following page:



An assumption implicit in this treatment is that only the partial rate factors for positions ortho to methyl groups are changed by steric interactions from the values predicted by the Additivity Principle. This means that the overall rate of substitution of any hydrocarbon containing one or more such positions should be less than the rate calculated from Additivity. No nitration studies are available to test this assumption, but the fact that rates of other reactions have been successfully predicted to within a factor of 2 while calculated isomer distributions in the same reactions bear no relationship to experimental values (Table VIII) means that the assumption may well be unjustified. However, the results in Table X (p. 46) show that at least in the protodetrimethylsilylation and mercuridetrimethylsilylation reactions the assumption is valid--e.g., the calculated and experimental rates for 4-R-m-xylene.

For any given position in a polymethylbenzene, the rate of substitution relative to one position in benzene is given by

$$\log k_i = \rho \sum_i \sigma_i^+$$

Writing σ_o, σ_m and σ_p in place of $\sigma^+_{o\text{-Me}}$, $\sigma^+_{m\text{-Me}}$ and $\sigma^+_{p\text{-Me}}$, the equations for the three positions in toluene are

$$\log k_o = \rho \sigma_o, \qquad \log k_m = \rho \sigma_m, \qquad \log k_p = \rho \sigma_p.$$

From these are obtained:

$$\log \frac{k_o}{k_m} = \rho (\sigma_o - \sigma_m) \quad \ldots\ldots\ldots\ldots \quad (1)$$

$$\log \frac{k_o}{k_p} = \rho (\sigma_o - \sigma_p) \quad \ldots\ldots\ldots\ldots \quad (2)$$

$$\log \frac{k_m}{k_p} = \rho (\sigma_m - \sigma_p) \quad \ldots\ldots\ldots\ldots \quad (3)$$

Since the k values are partial rate factors, $k_o/k_m = o_f/m_f$, $k_o/k_p = o_f/p_f$ and $k_m/k_p = m_f/p_f$, and the values of these ratios have been evaluated from the experimental results (Table L). σ_p and σ_m are given by Brown for nitration as -0.278 and -0.079 respectively,[145] and from equation (3) ρ for each nitrating system may be calculated. These values, with equations (1) or (2), allow σ_o to be calculated--the equations are not independent and the same result is obtained from each.

Similar equations may be written for the other hydrocarbons and these are listed in Table LV. Each set of equations may be solved by using the experimentally determined partial rate factor ratios (Table L) and the values of ρ calculated from the toluene results. The modified σ_o

TABLE LV

Equations for modified σ_o values[a]

o-xylene:

$\log k_3 = \rho(\sigma'_o + \sigma_m)$; $\log k_4 = \rho(\sigma_m + \sigma_p)$;

$\log k_3/k_4 = \rho(\sigma'_o - \sigma_p)$ . . . . . (4)

m-xylene:

$\log k_2 = \rho(2\sigma^*_o)$; $\log k_4 = \rho(\sigma_o + \sigma_p)$;

$\log k_2/k_4 = \rho(2\sigma^*_o - \sigma_o - \sigma_p)$;

hemimellitene:

$\log k_4 = \rho(\sigma''_o + \sigma_m + \sigma_p)$; $\log k_5 = \rho(2\sigma_m + \sigma_p)$;

$\log k_4/k_5 = \rho(\sigma''_o - \sigma_m)$

pseudocumene:

$\log k_3 = \rho(2\sigma^{**}_o + \sigma_m)$; $\log k_6 = \rho(\sigma'_o + 2\sigma_m)$;

$\log k_5 = \rho(\sigma_o + \sigma_m + \sigma_p)$;

$\log k_3/k_5 = \rho(2\sigma^{**}_o - \sigma_o - \sigma_p)$ . . . . . (5)

$\log k_3/k_6 = \rho(2\sigma^{**}_o - \sigma'_o - \sigma_m)$ . . . . . (6)

$\log k_5/k_6 = \rho(\sigma_o + \sigma_p - \sigma_m - \sigma'_o)$ . . . . . (7)

a) k_x refers to the partial rate factor for position x in the hydrocarbon.

values obtained are listed in Table LVI. The values of ρ will be subject to considerable error since the calculation of each involves the very small meta product in toluene and only one set of data. However, ρ appears in all equations and a consistent set of σ_o values should be obtained for each reaction system.

TABLE LVI

Modified σ_o values calculated from product distributions

Hydrocarbon		HNO_3-Ac_2O	NO_2BF_4	HNO_3-$MeNO_2$
toluene	ρ	-7.1 ± 0.2	-6.8 ± 0.2	-6.6 ± 0.2
	σ_o	-0.27 ± 0.02	-0.27 ± 0.02	-0.27 ± 0.02
o-xylene	σ_o'	-0.23 ± 0.02	-0.30 ± 0.03	-0.35 ± 0.03
m-xylene	σ_o^*	-0.24 ± 0.04	-0.24 ± 0.04	-0.24 ± 0.04
hemimellitene	σ_o''	-0.15 ± 0.04	-0.14 ± 0.04	-0.20 ± 0.04
pseudocumene	σ_o^{**}	-0.22 -0.18	-0.19 -0.14	-0.22 -0.17
	Mean	-0.20	-0.17	-0.20
	σ_o'	-0.32	-0.40	-0.43

Discussion of Table LVI

ρ -Values. The values obtained for the three reaction systems are the same within experimental error, and are comparable to Brown's value of -6.0 obtained from composite data for nitration under several conditions. The nitronium tetrafluoroborate reaction shows the same value of ρ as the other two systems in accordance with Olah's observation that "normal" intramolecular selectivity is preserved in these reactions. Nitration in nitric acid-acetic anhydride mixtures displays similar selectivity to the other systems. If the "Read" protonated acetyl nitrate (species III, p. 149) is the nitrating entity in this system it does not display the low selectivity often associated with highly polar species.

σ_o-Values are the same in the three nitrating systems. The value of -0.27 is close to the value of $\sigma^+_{p\text{-Me}}$ = -0.278 found by Brown for the nitration reaction,[145] and to the values obtained by McGary for $\sigma^+_{o\text{-Me}}$ for chlorination, nitration and HF-BF_3 basicity of -0.275, -0.274 and -0.277 respectively.[150] The constancy of the values for the three nitrating systems indicates that steric interactions between the methyl group and each of the three electrophiles are very similar. In fact the methyl group is probably too small to interact significantly with the electrophile entering the ortho position, and the σ_o

values will thus be a true measure of the combined inductive and electromeric effects of the methyl group in the ortho position. Such effects should be the same in the three nitrating systems because the ρ values are the same.

σ_o^* values for m-xylene are constant and just significantly lower than the σ_o values for toluene. This is consistent with enhanced steric inhibition at the 2-position by the flanking methyl groups; the constant value in this case must indicate that the three electrophiles have similar steric requirements when attacking at the 2-position in m-xylene.

σ_o'' values from hemimellitene are significantly lower than the σ_o and σ_o^* values, and also lower than the σ_o' value obtained for o-xylene from nitration in nitric acid-acetic anhydride mixtures. The steric effect of a double-buttressed methyl group thus appears to be larger than either the buttressed methyl or the two single methyls in m-xylene.

σ_o^{**} values may be obtained from equations (5) and (6) using either the σ_o' values from o-xylene or those obtained from equation (7). Both values are shown in Table LVI with the mean value. The mean values are constant within experimental error and probably slightly higher than the σ_o'' values but the errors involved in the calculations make it difficult to judge whether the differences between σ_o^{**} and σ_o'' values are significant.

σ_o' values reflect the effect discussed in the previous section (p. 169). The value from o-xylene for the nitric acid-acetic anhydride system is significantly lower than σ_o, indicating steric inhibition of attack at the 3-position. The values from o-xylene for the other two systems are very much higher than σ_o. The σ_o' values from pseudocumene are all higher than σ_o, but the value for the nitric acid-acetic anhydride system is considerably lower than those for the other systems. These results are discussed qualitatively on p. 169.

Conclusion

Because the modified σ_o values obtained from the nitric acid-acetic anhydride results, for the hydrocarbons more activated than o-xylene, are consistent with those from the other two nitrating systems, it is assumed that the first order nitration reaction taking place in these compounds (p. 153) does not significantly affect the product distributions. This assumption will be correct if the species responsible for the first order nitration has the same selectivity and steric requirements as the species responsible for acetoxylation and zeroth order nitration. Although the ρ values for the two reactions cannot be identical, ρ values for different nitrating species are usually very similar (cf. this work and reference 145), and the first requirement is likely to be very nearly met. If

the first order species is one of the other protonated acetyl nitrates, then the steric requirement will also be met.

It is clear from this study that the NO_2BF_4-sulpholane nitrations give product distributions almost the same as those from the other two nitrating systems. No conclusions about the mechanism of this reaction can be made from this work, but Olah's claim that "normal" intramolecular selectivity is retained in these reactions has been shown to be correct for all the hydrocarbons studied.

The modified σ_o values obtained are not likely to be suitable for use with other reactions unless the attacking electrophile has steric requirements similar to those of the electrophiles in the systems studied. Further, the values of σ_o are not particularly sensitive to small changes in product distribution; the usual order of precision in the determination of σ^+ values for a given substituent over a range of reactions is ± 0.3,[145] and the widest variation in the results obtained for all the modified σ_o values except σ_o' is only twice this figure. This, together with the low precision with which the modified σ_o values can be calculated, makes such values of little practical use in predicting product ratios.

The results demonstrate that the Additivity Principle cannot be used to calculate isomer distributions for these

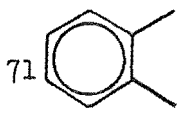
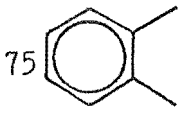
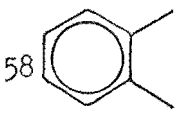
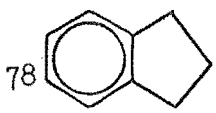
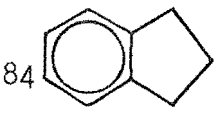
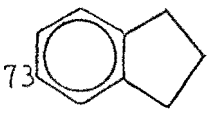
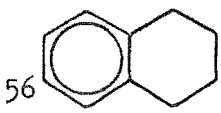
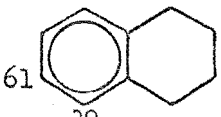
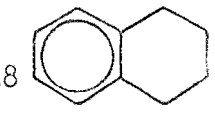
hydrocarbons in the three systems studied. It seems very likely that the same conclusion would be reached for other reactions, and that calculations of product ratios based on Additivity are likely to be misleading rather than helpful.

The Mills-Nixon Effect

Nitration reactions have ρ values lower than a number of other electrophilic substitutions, and are less suitable for investigating an effect likely to involve small differences in transition state stabilities than are reactions such as bromination which can have higher ρ values and thus higher selectivity. For this reason the product distributions resulting from the bromination of indan, tetralin and o-xylene[151] were determined in collaboration with G.J. Welch, and the results of this study are given in Table LVII. The

TABLE LVII

Bromination results from the work of Welch and Wright
(percent total bromo-products)

Br_2-AcOH	Br_2-85% AcOH aq.	BrOH-AcOH
 71 / 29	 75 / 25	 58 / 42
 78 / 22	 84 / 16	 73 / 27
 56 / 44	 61 / 39	 48 / 52

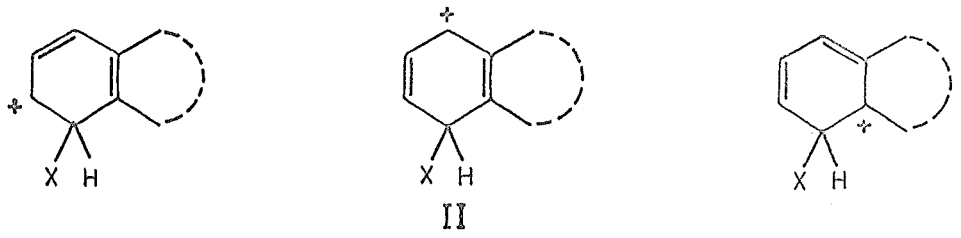
nitration results are best discussed in terms of the explanation offered by Welch and Wright for the brominations, and this explanation is outlined below.

The bromination results show that the product distributions are not governed by a primary steric effect. Molecular models show that the methylene groups adjacent to the benzene ring offer more hindrance to ortho attack in tetralin than they do in indan. Arnold et al.[152] have obtained considerable physical and chemical evidence to support this view. If such a steric effect were the major factor determining the product distribution, more ar- β product would be formed in tetralin than in indan. In fact, as the results show, tetralin gives less ar- β product. Presumably such a steric effect does operate, but it is outweighed by another factor.

Attempts have been made to explain the Mills-Nixon effect in terms of differences between the effectiveness of hyperconjugative release from the methylene groups to the benzene ring in indan and tetralin. Berthier and Pullman[114] attempt to explain the predominance of ar- β product in these compounds by such differences. It has been shown in the introduction, however, that their conclusion that ar-β substitution predominates is based on inconclusive evidence, and the bromination results in Table LVII show that the amount of ar- α product may well be greater than the

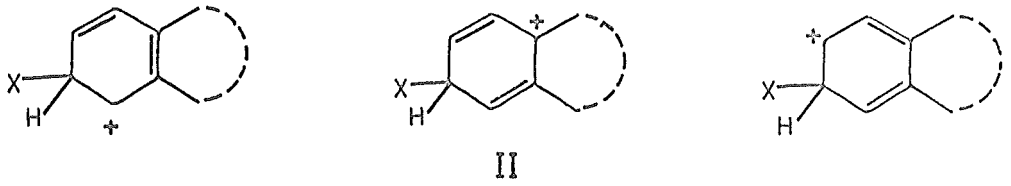
amount of ar-β . Furthermore, there is doubt about the relative effectiveness of hyperconjugation in the two compounds. In indan the C-H bonds of the methylene groups adjacent to the ring are ideally oriented for hyperconjugation with the ring, but no C-C hyperconjugation can occur. In tetralin, the methylenes are less favourably oriented for C-H release, but C-C hyperconjugation can occur. It is generally assumed, and the spectroscopic evidence of Moore et al.[153] is usually interpreted to mean, that hyperconjugation is more effective in tetralin than in indan. Dewar[154] has pointed out that the interpretation of the experimental evidence in terms of hyperconjugation in these compounds is open to serious doubt.

Examination of the resonance forms contributing to the transition states for ar- α and ar- β substitution in any ortho-di-substituted benzene shows that preferential stabilisation by any charge-spreading such as hyperconjugation can have no effect on the product ratio. If the transition state in each case is assumed to approximate to the σ - complex, the relevant resonance forms are likely to approximate to the following:



II

ar-α substitution



II

ar-β substitution

Examination of these two sets of resonance forms shows that the formal positive charges occur in the same positions relative to the fused alicycle in both types of substitution. When the alternative position of substitution in each case is considered, it is evident that in moving from the ground state to the transition state the change in charge at any given carbon atom is the same for both types of substitution. Thus, preferential stabilisation of the transition state in one of the hydrocarbons by any mechanism such as hyper-conjugation should affect both positions of substitution

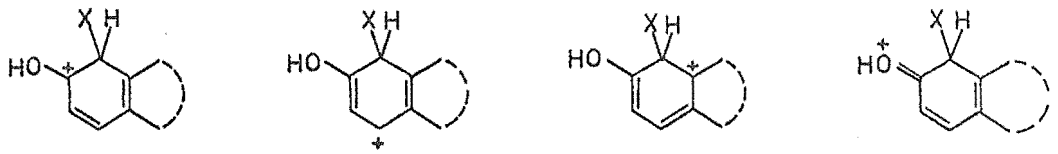
equally, and thus increase the overall rate of substitution for that hydrocarbon without affecting the product distribution.

There is one significant difference between the two sets of resonance forms, however. In ar- α substitution, the bond common to the two rings has effectively $\frac{2}{3}$ double bond character, while in ar- β substitution it has effectively $\frac{1}{3}$ double bond character. In discussions of the Mills-Nixon effect it has generally been assumed that increasing the double bond character of this bond in the ground state of indan will result in a less stable system because of the increased strain in the alicyclic ring, while in tetralin an increase in stability will result. The review by Brown et al.[155] of reactions involving the formation of five- and six-membered rings containing endo and exo double bonds supports this assumption. Brown concludes that "reactions will proceed in such a manner as to favour the formation or retention of an exo double bond in the 5-ring, and to avoid the formation or retention of the exo double bond in the 6-ring". The comparison above indicates that these differences become important in forming the transition states, and that indan should favour ar- β attack and tetralin ar- α attack. On the basis of this comparison, o-xylene might be expected to give product distributions intermediate between those of indan and tetralin, since the constraint imposed by

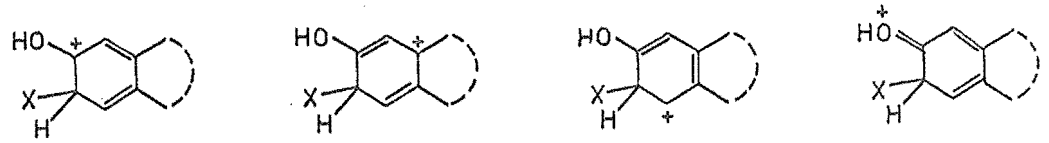
the fused ring is not present. The bromination results show this to be the case.

An assumption implicit in this explanation is that the three resonance forms contribute approximately equally to the transition state for each substitution type. It is likely in fact that the p-quinonoid structures (II) will make a larger contribution than the other two forms in each case.[156] Also, forms with a single common bond will be destabilised in tetralin and those with a double common bond will be destabilised in indan. Both effects operate in the direction required for this explanation.

The original results of Mills and Nixon may be accounted for in terms of this explanation. The resonance forms for the two transition states are



ar- α substitution



ar- β substitution

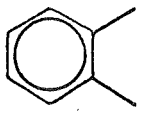
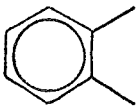
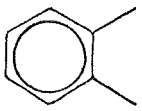
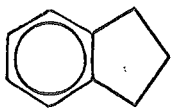
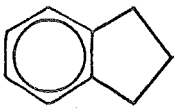
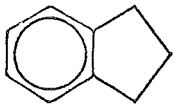
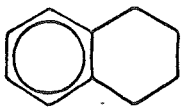
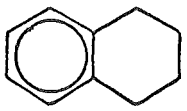
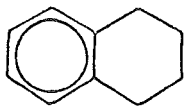
These now include a fourth form involving a positively-charged phenol group, giving $\frac{3}{4}$ double bond character to the common bond in ar- α substitution and $\frac{1}{4}$ double bond character in ar- β substitution. Whether or not the extra resonance forms make contributions to the transition states equal to or greater than the other forms, in each case the effect on the common bond is such that ar- α attack should be strongly favoured in 6-tetralol to give the 5-product, and ar- β attack be favoured in 5-indanol to give the 6-product. This is the result found by Mills and Nixon.

The nitration results

The product distributions from the nitrations of indan, tetralin and o-xylene are summarised in Table LVIII. The table shows that the nitric acid-acetic anhydride system gives results very similar to those obtained from the bromination reactions, but the differences between the three hydrocarbons are less marked because of the lower selectivity of the nitration reaction. The distributions obtained from the other two nitrating systems do not conform to the pattern. It is suggested that this results from the same effect, discussed in the previous section, leading to abnormally high amounts of 3-nitro-o-xylene and 6-nitro-pseudocumene from nitrations in nitric acid-nitromethane mixtures and NO_2BF_4-sulpholane mixtures. The effect in

TABLE LVIII

Product distributions for nitration:
indan, tetralin and o-xylene
(percent total nitro-products)

HNO_3-Ac_2O	NO_2BF_4-sulpholane	HNO_3-$MeNO_2$
67·4  32·6	26·3  73·7	41·6  58·4
73·9  26·1	41·7  58·3	58·1  41·9
64.9  35·1	38·6  61·4	58.7  41·3

o-xylene is to increase the amount of ar- α product; indan and tetralin both show much higher proportions of ar- α product in these two systems than in the bromination reactions or in nitric acid-acetic anhydride nitrations. In the NO_2BF_4-sulpholane system, application of Student's "t" test to the results for indan and tetralin shows that the difference between the percentage of ar- α product for the two compounds (58.3% and 61.4%) is significant (t=4.56), and

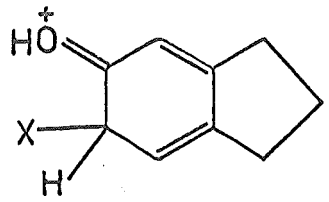
in the required direction. However, when compared with the bromination results, the difference is barely appreciable. The difference in the nitric acid-nitromethane system is not significant, and that found by Tanida and Muneyuki[119] (Table XII) for nitration in nitric acid-nitromethane mixtures of unspecified composition (50%, 48.4%), is likewise barely significant.

If Olah's proposed π -complex mechanism for nitrations in NO_2BF_4-sulpholane mixtures is correct, the explanation outlined above in terms of σ -complex transition state stabilities is not valid for such reactions, since the rate-determining transition state is far removed from the σ -complex. If this is the case, the ground state configuration of the hydrocarbons will be important in determining the product distributions. According to the charge density calculations made by Berthier and Pullman,[114] (p. 190) the ar- β carbons in both indan and tetralin have higher charges than the ar- α carbons and thus the NO_2BF_4 nitrations might be expected to give more ar- β product than ar-α . Two factors must be noted; firstly Berthier and Pullman assume significant hyperconjugation in the ground state of these molecules, which is not likely, and their results must be accepted with reserve, and secondly, the effect operating in o-xylene to increase the proportion of 3-isomer above the expected value may also be operating

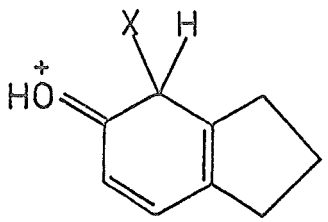
in indan and tetralin.

Quantum mechanical and other treatments

In their quantum mechanical treatment of indan,[113] Longuet-Higgins and Coulson calculate the bond lengths of the hydrocarbon in the ground state and then, assuming these to be unchanged in 5-indanol, compare the energies of activation of the two resonance forms III and IV. The bonds in the aromatic ring attached to the tetrahedral carbon atom will be longer than normal aromatic bonds, and examination of the calculated bond lengths for the ground state molecule shows that III will be more readily formed and therefore



III



IV

more stable than IV, since the bond distortions required to form III are smaller than those required to form IV. This treatment correctly predicts the orientation in 5-indanol although it ignores the other resonance forms. These workers did not examine the corresponding tetralol. Berthier and Pullman calculate the ground state configurations for indan and tetralin. Their calculated bond orders

for the aromatic bonds in both hydrocarbons are such that application of the Longuet-Higgins argument leads to the conclusion that both 5-indanol and 6-tetralol should substitute in equivalent positions (the 6- and 7-positions respectively). However, Berthier and Pullman also calculate the ground state configuration of the two phenols and find that although the two have similar geometry, the pattern of aromatic bond orders is quite different from that of the parent hydrocarbons. Application of the Longuet-Higgins argument in this case leads again to the conclusion that both phenols should be attacked in equivalent positions, but this time probably in the 4- and 5-positions. Clearly this approach is of little value until more reliable calculations can be made.

Berthier and Pullman also calculate the charge densities at the benzene ring carbon atoms in both the parent hydrocarbons and the phenols. They assume that the position of highest charge density will give the largest amount of product, predict that both hydrocarbons will give predominantly β -substitution, and explain the orientation in the phenols. However, because the stability of the transition states is affected by the fused alicyclic ring systems this simple argument cannot be used to predict product distributions. In fact, as the bromination results show, β -substitution does not necessarily predominate.

The authors comment that "a second treatment is desirable, interpreting the chemical facts by transition state theory".

Pascual has recently examined the results of Mills and Nixon and shown that a combination of polar and steric factors will explain the experimental results, but it seems doubtful whether these factors alone will account for the almost complete specificity of the substitution reactions for these phenols. Any such effects must operate in addition to the explanation already given, and Pascual's analysis is able to explain the orientation in 3,4-xylenol, which has no fused ring system. It cannot however be applied to the unsubstituted hydrocarbons.

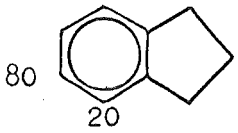
Other results

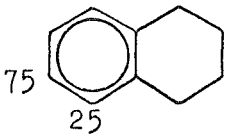
Granger et al. have determined the product distributions from chloromethylation of indan and tetralin, and from Friedel-Crafts cyclisations of o-xylene-, indan-, and tetralin-3-propionyl chlorides and 3-(phenyl-3)-propionyl chlorides. These results are summarised in Table LIX. The chloromethylation results parallel the nitration results for nitric acid-acetic anhydride mixtures and may be explained in the same way. The cyclisation results fall into the same order as the bromination results (Table LVII), but show much larger differences between indan and tetralin.

TABLE LIX

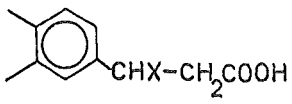
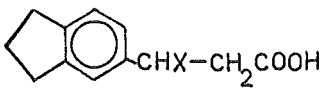
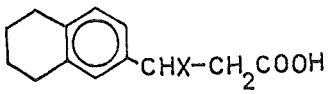
Product distributions from the work of Granger et al.

A Chloromethylations (percentages)





B Friedel-Crafts cyclisations

	X = H		X = phenyl	
	% α	% β	% α	% β
	35	65	17	83
	10	90	20	80
	75	25	90	10

If these results reflect the transition state stabilities and not product stabilities, the larger differences may be due at least in part to the high value of ρ (-9.1) for acetylation.

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